U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: _____ Serial Number: _____

Date: _____ Phone: _____ Art Unit: _____

Search Topic:
Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

STAFF USE ONLY

Date completed: 06-27-02
Searcher: Beverly e 4994
Terminal time: _____
Elapsed time: _____
CPU time: _____
Total time: _____
Number of Searches: _____
Number of Databases: _____

Search Site
_____ STIC
_____ CM-1
_____ Pre-S

Type of Search
_____ N.A. Sequence
_____ A.A. Sequence
_____ Structure
_____ Bibliographic

Vendors
_____ IG
✓ STN
✓ Dialog
_____ APS
_____ Geninfo
_____ SDC
_____ DARC/Questel
_____ Other

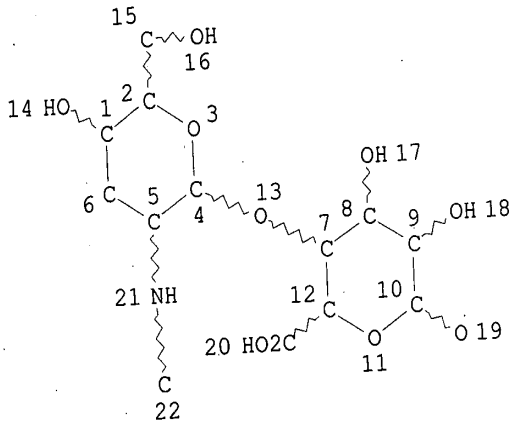
001

Devi, S.
09/853367

FILE 'REGISTRY' ENTERED AT 11:20:12 ON 27 JUN 2002

L1 STR

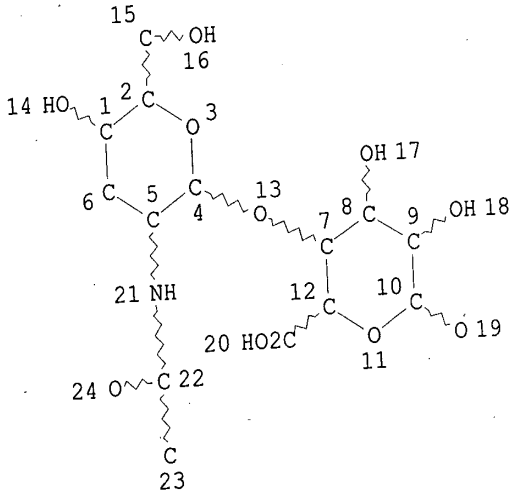
Str.



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L2 (235) SEA FILE=REGISTRY SSS FUL L1
L3 STR

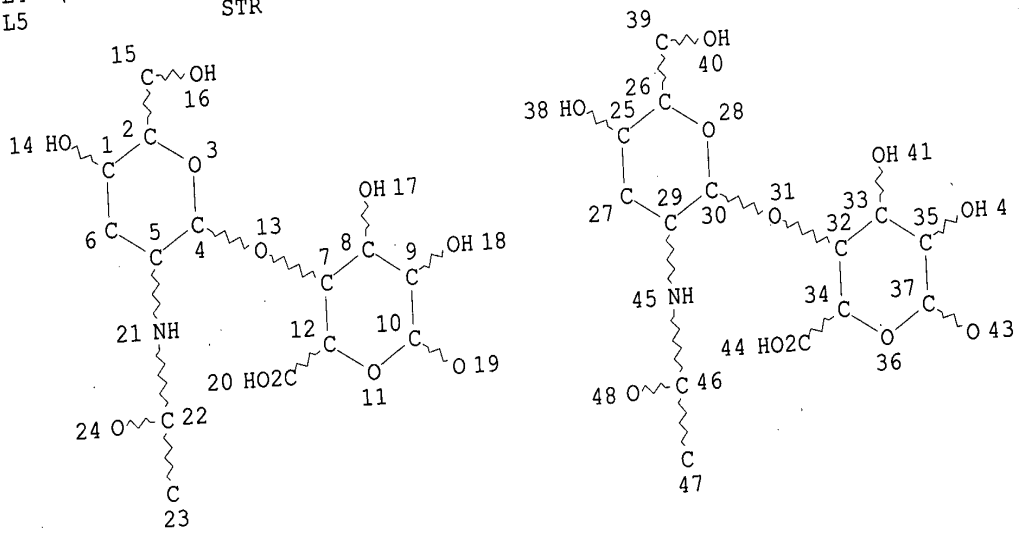


NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

Searcher : Shears 308-4994

STEREO ATTRIBUTES: NONE
L4 (235) SEA FILE=REGISTRY SUB=L2 SSS FUL L3
L5 STR



Page 1-A

2

Page 1-B
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 48

STEREO ATTRIBUTES: NONE
L6 95 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L7 66 SEA FILE=REGISTRY ABB=ON PLU=ON L6 AND 1/NC

(FILE 'HCAPLUS' ENTERED AT 11:23:10 ON 27 JUN 2002)
L8 38 S L7 OR L7/D

E1 THROUGH E69 ASSIGNED

L8 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:527081 HCAPLUS
DOCUMENT NUMBER: 135:224291
TITLE: The nematode Caenorhabditis elegans synthesizes unusual O-linked glycans: identification of glucose-substituted mucin-type O-glycans and short chondroitin-like oligosaccharides
AUTHOR(S): Guerardel, Yann; Balanzino, Luis; Maes, Emmanuel; Leroy, Yves; Coddeville, Bernadette; Oriol, Rafael; Strecker, Gerard
CORPORATE SOURCE: Laboratoire de Chimie Biologique et Unite Mixte de Recherche du CNRS 8576, Universite des

Sciences et Technologies de Lille, Villeneuve d'Ascq, F-59655, Fr.
SOURCE: Biochemical Journal (2001), 357(1), 167-182
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The free-living nematode Caenorhabditis elegans is a relevant model for studies on the role of glycoconjugates during development of multicellular organisms. Several genes coding for glycosyltransferases involved in the synthesis of N- and O-linked glycans have already been isolated, but, apart from repetitive dimers of glycosaminoglycans, no detailed structure of either type of component has been published so far. This study aimed to establish the structures of the major O-glycans synthesized by C. elegans to give an insight into the endogenous glycosyltransferase activities expressed in this organism. By the use of NMR and MS, we have resolved the sequence of seven of these components that present very unusual features. Most of them were characterized by the type-1 core substituted on Gal and/or GalNAc by (.beta.1-4)Glc and (.beta.1-6)Glc residues. Another compd. exhibited the GalNAc(.beta.1-4)N-acetylglucosaminitol sequence in the terminal position, to which was attached a tetramer of .beta.-Gal substituted by both Fuc and 2-O-methyl-fucose residues. Our exptl. procedure led also to the isolation of glycosaminoglycan-like components and oligomannosyl-type N-glycans. In particular, the data confirmed that C. elegans synthesizes the ubiquitous linker sequence GlcA(.beta.1-3)Gal(.beta.1-3)Gal(.beta.1-4)Xyl.

IT **199943-21-0P**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(identification of glucose-substituted mucin-type O-glycans and short chondroitin-like oligosaccharides of nematode)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:330845 HCAPLUS
DOCUMENT NUMBER: 135:137661
TITLE: Synthesis of linear-type chondroitin clusters having a C8 spacer between disaccharide moieties and enzymatic transfer of D-glucuronic acid to the artificial glycans

AUTHOR(S): Tamura, Jun-ichi; Urashima, Hirofumi; Tsuchida, Kazunori; Kitagawa, Hiroshi; Sugahara, Kazuyuki
CORPORATE SOURCE: Faculty of Education and Regional Sciences, Department of Environmental Sciences, Tottori University, Tottori, 680-8551, Japan

SOURCE: Carbohydrate Research (2001), 332(1), 41-51
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Newly designed linear-type glycoclusters were synthesized which involve a chondroitin repeating disaccharide ligand and a hydrophobic octyl ether spacer. The spacer mimics the corresponding

disaccharide unit. Repeating elongation of the pseudo-tetrasaccharide that was derived from the common cluster unit [.fwdarw.8)-octyl-(1.fwdarw.3)-.beta.-D-GalNAc-(1.fwdarw.4)-.beta.-D-GlcA-(1.fwdarw.] allowed the syntheses of up to the pseudo-decasaccharide analog of chondroitin. An enzymic D-GlcA transfer at the non-reducing end of the synthesized artificial glycans by GlcATase II was obsd.

IT **352210-48-1DP**, glucuronosylated **352210-49-2DP**, glucuronosylated
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of C8-spaced chondroitin glycoclusters and their receptor activity toward GlcATase II)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:468056 HCAPLUS
DOCUMENT NUMBER: 133:99567
TITLE: Glucuronate and glucosamine derivatives-containing compounds as leukocyte-vascular endothelial cell adhesion inhibitors
INVENTOR(S): Yatsuka, Nobuaki; Sato, Nobuyuki; Moriyama, Shigeru; Tamai, Tadakazu; Nishikawa, Masazumi
PATENT ASSIGNEE(S): Maruha Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000191538	A2	20000711	JP 1998-372864	19981228

OTHER SOURCE(S): MARPAT 133:99567

AB Glucuronate and glucosamine derivs.-contg. compds. (Markush's structures given) are claimed as leukocyte-vascular endothelial cell adhesion inhibitors for treatment of ischemia-reperfusion injury and inflammatory diseases. Formulation examples of tablets, capsules, suspensions, suppositories, and injections were given.

IT **198191-91-2P 198191-93-4P 198191-95-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)

L8 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:419926 HCAPLUS
DOCUMENT NUMBER: 133:204476
TITLE: Conformational behavior of hyaluronan in relation to its physical properties as probed by molecular modeling
AUTHOR(S): Haxaire, Katia; Braccini, Isabelle; Milas, Michel; Rinaudo, Marguerite; Perez, Serge

CORPORATE SOURCE: Centre de Recherches sur les Macromolecules Vegetales, CNRS (associated with Universite Joseph Fourier, Grenoble, Grenoble, 38041, Fr.

SOURCE: Glycobiology (2000), 10(6), 587-594
CODEN: GLYCE3; ISSN: 0959-6658
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hyaluronan (HA) is a linear charged polysaccharide whose structure is made up of repeating disaccharide units. Apparently conflicting reports have been published about the nature of the helical structure of HA in the solid state. Recent developments in the field of mol. modeling of polysaccharides offer new opportunities to reexamine the structural basis underlying the formation and stabilization of ordered structures and their interactions with counterions. The conformational spaces available and the low energy conformations for the disaccharide, trisaccharide, and tetrasaccharide segments of HA were investigated via mol. mechanics calcns. using the MM3 force field. First, the results were used to access the configurational statistics of the corresponding polysaccharide. A disordered chain having a persistence length of 75 .ANG. at 25.degree. is predicted. Then, the exploration of the stable ordered forms of HA led to numerous helical conformations, both left- and right-handed, having comparable energies. Several of these conformations correspond to the exptl. obsd. ones and illustrate the versatility of the polysaccharide. The double stranded helical forms have also been explored and theor. structures have been compared to exptl. derived ones.

IT **216065-16-6**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(repeating unit of; conformational behavior of hyaluronan in relation to its phys. properties as probed by mol. modeling)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:359553 HCAPLUS
DOCUMENT NUMBER: 133:131564
TITLE: Chimeric glycosaminoglycan oligosaccharides synthesized by enzymatic reconstruction and their use in substrate specificity determination of Streptococcus hyaluronidase
AUTHOR(S): Takagaki, Keiichi; Munakata, Hidekazu; Majima, Mitsuo; Kakizaki, Ikuko; Endo, Masahiko
CORPORATE SOURCE: Department of Biochemistry, Hirosaki University School of Medicine, Hirosaki, 036-8562, Japan

SOURCE: Journal of Biochemistry (Tokyo) (2000), 127(4), 695-702
CODEN: JOBIAO; ISSN: 0021-924X
PUBLISHER: Japanese Biochemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A method was developed for the reconstruction of glycosaminoglycan (GAG) oligosaccharides using the transglycosylation reaction of an endo-.beta.-N-acetylhexosaminidase, testicular hyaluronidase, under optimal conditions. Repetition of the transglycosylation using

suitable combinations of various GAGs as acceptors and donors made it possible to custom-synthesize GAG oligosaccharides. Thus we prepd. a library of chimeric GAG oligosaccharides with hybrid structures composed of disaccharide units such as GlcA-GlcNAc (from hyaluronic acid), GlcA-GalNAc (from chondroitin), GlcA-GalNAc4S (from chondroitin 4-sulfate), GlcA-GalNAc6S (from chondroitin 6-sulfate), IdoA-GalNAc (from desulfated dermatan sulfate), and GlcA-GalNAc4,6-diS (from chondroitin sulfate E). The specificity of the hyaluronidase from Streptococcus dysgalactiae (hyaluronidase SD) was then investigated using these chimeric GAG oligosaccharides as model substrates. The results indicate that the specificity of hyaluronidase SD is detd. by the following restrictions at the nonreducing terminal side of the cleavage site: (i) at least one disaccharide unit (GlcA-GlcNAc) is necessary for the enzymic action of hyaluronidase SD; (ii) cleavage is inhibited by sulfation of the N-acetylgalactosamine; (iii) hyaluronidase SD releases GlcA-GalNAc and IdoA-GalNAc units as well as GlcA-GlcNAc. At the reducing terminal side of the cleavage site, the sulfated residues on the N-acetyl-galactosamines in the disaccharide units were found to have no influence on the cleavage. Addnl., we found that hyaluronidase SD can specifically and endolytically cleave the internal unsulfated regions of chondroitin sulfate chains. This demonstration indicates that custom-synthesized GAG oligosaccharides will open a new avenue in GAG glycotechnol.

IT **73603-40-4P 101205-01-0P 286427-30-3P**
286427-32-5P 286427-33-6P 286427-34-7P
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(chimeric glycosaminoglycan oligosaccharide synthesized by enzymic reconstruction)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:325329 HCAPLUS
DOCUMENT NUMBER: 133:100965
TITLE: Increased incidence of unsulfated and 4-sulfated residues in the chondroitin sulfate linkage region observed by high-pH anion-exchange chromatography
AUTHOR(S): Lauder, Robert M.; Huckerby, Thomas N.; Nieduszynski, Ian A.
CORPORATE SOURCE: Department of Biological Sciences, Lancaster University, Lancaster, LA1 4YQ, UK
SOURCE: Biochemical Journal (2000), 347(2), 339-348
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We report the isolation, characterization and quantification of five octasaccharides, four hexasaccharides and two tetrasaccharides, derived from the chondroitin sulfate (CS) linkage region of 6-8-yr-old bovine articular cartilage aggrecan, following digestion with chondroitin ABC endolyase. Using a novel high-pH anion-exchange chromatog. (HPAEC) method, in conjunction with one- and two-dimensional 1H-NMR spectroscopy, we have identified the

following basic structure for the CS linkage region of aggrecan: .DELTA.UA(.beta.1-3)GalNAc[0S/4S/6S](.beta.1-4)GlcA(.beta.1-3)GalNAc[0S/4S/6S](.beta.1-4)GlcA(.beta.1-3)Gal[0S/6S](.beta.1-3)Gal(.beta.1-4)Xyl, where .DELTA.UA represents 4,5-unsatd. hexuronic acid, and 4S and 6S represent an O-ester sulfate group on C-4 and C-6 resp. The octa-, hexa- and tetra-saccharide linkage region fragments were used to develop a HPAEC fingerprinting method, with detection at A232nm, and a linear response to approx. 0.1 nmol of substance. The sulfation patterns of CS linkage regions, of up to octasaccharide in size, from articular and tracheal cartilage aggrecan were examd. The results show that in articular cartilage, for the majority (53%) of octasaccharides the 2-deoxy-2-N-acetyl amino-D-galactose (GalNAc) residues closest to the linkage region are both 6-sulfated; however, in a significant portion (34%), one or more of these GalNAc residues are unsulfated, and in 8% both are unsulfated. Approx. 10-18% of the chains have a 4-sulfated GalNAc in the first disaccharide, and 12% have a sulfated linkage region Gal residue. No evidence was found for uronic acid sulfation. These data show that there is a significant increase in the incidence of unsulfated and 4-sulfated GalNAc residues adjacent to the linkage region compared with the rest of the chain. Bovine tracheal cartilage linkage regions displayed very similar sulfation profiles to those from articular cartilage, despite the presence of a higher level of GalNAc 4-sulfation within the repeat region of the main CS chain.

IT **220222-62-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(increased incidence of unsulfated and 4-sulfated residues in the chondroitin sulfate linkage region obsd. by high-pH anion-exchange chromatog.)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:224976 HCAPLUS
DOCUMENT NUMBER: 133:116563
TITLE: Enzymatic Reconstruction of Dermatan Sulfate
AUTHOR(S): Takagaki, Keiichi; Munakata, Hidekazu; Kakizaki, Ikuko; Majima, Mitsuo; Endo, Masahiko
CORPORATE SOURCE: Department of Biochemistry, Hirosaki University School of Medicine, Hirosaki, 036-8562, Japan
SOURCE: Biochemical and Biophysical Research Communications (2000), 270(2), 588-593
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We investigated the enzymic reconstruction of dermatan sulfate (DS) using the transglycosylation reaction of testicular hyaluronidase. First, in order to insert the IdoA-GalNAc disaccharide unit into chondroitin sulfate chains consisting of GlcA-GalNAc disaccharide units, desulfated DS as a donor and pyridylaminated (PA) chondroitin 6-sulfate (Ch6S) hexasaccharide as an acceptor were subjected to a transglycosylation reaction using testicular hyaluronidase. The products were analyzed by HPLC, mass spectrometry, and enzymic digestions, and the results indicated that one of the products was

IdoA-GalNAc-(GlcA-GalNAc6S)3-PA. Next, when the resulting PA-Ch6S (hexa-)desulfated DS (di-)octasaccharide was used as an acceptor and chondroitin as a new donor, a decasaccharide having a GlcA-GalNAc-IdoA-GalNAc-(GlcA-GalNAc6S)3 sequence was reconstructed. Using suitable combinations of donors and acceptors, it was possible to custom synthesize DS having any IdoA sequence as its uronic acid component. It is likely that application of this system would facilitate artificial reconstruction of variant DS having different specific functions. (c) 2000 Academic Press.

IT **285560-07-8P 285560-09-0P 285560-10-3P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(enzymic reconstruction of dermatan sulfate using transglycosylation by testicular hyaluronidase)

IT **285560-11-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(enzymic reconstruction of dermatan sulfate using transglycosylation by testicular hyaluronidase)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:348950 HCAPLUS
DOCUMENT NUMBER: 131:196215
TITLE: Substrate specificity studies of Flavobacterium chondroitinase C and heparitinases towards the glycosaminoglycan-protein linkage region. Use of a sensitive analytical method developed by chromophore-labeling of linkage glycoserines using dimethylaminoazobenzenesulfonyl chloride
AUTHOR(S): Tsuda, Hiromi; Yamada, Shuhei; Miyazono, Hirofumi; Morikawa, Kiyoshi; Yoshida, Keiichi; Goto, Fumitaka; Tamura, Jun-Ichi; Neumann, Klaus W.; Ogawa, Tomoya; Sugahara, Kazuyuki
CORPORATE SOURCE: Department of Biochemistry, Kobe Pharmaceutical University, Kobe, 658-8558, Japan
SOURCE: European Journal of Biochemistry (1999), 262(1), 127-133
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacterial chondroitinases and heparitinases are potentially useful tools for structural studies of chondroitin sulfate and heparin/heparan sulfate. Substrate specificities of Flavobacterium chondroitinase C, as well as heparitinases I and II, towards the glycosaminoglycan-protein linkage region -HexA-HexNAc-GlcA-Gal-Gal-Xyl-Ser (where HexA represents glucuronic acid or iduronic acid and HexNAc represents N-acetylgalactosamine or N-acetylglucosamine) were investigated using various structurally defined oligosaccharides or oligosaccharide-serines derived from the linkage region. In the case of oligosaccharide-serines, they were labeled with a chromophore dimethylaminoazobenzenesulfonyl chloride (DABS-Cl), which stably reacted with the amino group of the serine residue and

rendered high absorbance for microanal. Chondroitinase C cleaved the GalNAc bond of the pentasaccharides or hexasaccharides derived from the linkage region of chondroitin sulfate chains and tolerated sulfation of the C-4 or C-6 of the GalNAc residue and C-6 of the Gal residues, as well as 2-O-phosphorylation of the Xyl residue. In contrast, it did not act on the GalNAc-GlcA linkage when attached to a 4-O-sulfated Gal residue. Heparitinase I cleaved the innermost glucosaminidic bond of the linkage region oligosaccharide-serines of heparin/heparan sulfate irresp. of substitution by uronic acid, whereas heparitinase II acted only on the glucosaminidic linkages of the repeating disaccharide region, but not on the innermost glucosaminidic linkage. These defined specificities of chondroitinase C, as well as heparitinases I and II, will be useful for prepn. and structural anal. of the linkage oligosaccharides.

IT **199943-20-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(substrate specificity studies of Flavobacterium chondroitinase C and heparitinases I and II towards glycosaminoglycan-protein linkage region using chromophore dimethylaminoazobenzenesulfonyl chloride derivatized to serine)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:300046 HCAPLUS
DOCUMENT NUMBER: 131:157882
TITLE: Enzymatic Reconstruction of a Hybrid Glycosaminoglycan Containing 6-Sulfated, 4-Sulfated, and Unsulfated N-Acetylgalactosamine
AUTHOR(S): Takagaki, Keiichi; Munakata, Hidekazu; Majima, Mitsuo; Endo, Masahiko
CORPORATE SOURCE: Department of Biochemistry, Hirosaki University School of Medicine, Hirosaki, 036-8562, Japan
SOURCE: Biochemical and Biophysical Research Communications (1999), 258(3), 741-744
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using the transglycosylation reaction of testicular hyaluronidase, reconstructions of hybrid glycosaminoglycans (GAGs) contg. 6-sulfated (GalNAc6S), 4-sulfated (GalNAcS) and unsulfated N-acetylgalactosamine (GalNAc) were investigated. First, chondroitin 4-sulfate (Ch4S) as a donor contg. GalNAc4S and the pyridylaminated (PA) chondroitin 6-sulfate (Ch6S) hexasaccharide as an acceptor contg. GalNAc6S were subjected to transglycosylation reaction. Second, when the resulting PA-Ch6S(hexa-)-Ch4S(di-)octasaccharide and chondroitin (Ch) were used as an acceptor and as a donor contg. GalNAc, resp., a new decasaccharide having a hybrid structure composed of disaccharide units derived from Ch6S, Ch4S and Ch was reconstructed. Using a systematic combination of each donor and acceptor mol., it was possible to reconstruct various types of hybrid GAGs. (c) 1999 Academic Press.

IT **237058-87-6P 237058-88-7P**
RL: ANT (Analyte); PNU (Preparation, unclassified); ANST (Analytical study); PREP (Preparation)

(enzymic reconstruction of hybrid glycosaminoglycans contg. 6-sulfated, 4-sulfated, and unsulfated N-acetylgalactosamine)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:35714 HCAPLUS
DOCUMENT NUMBER: 130:206504
TITLE: Deducing polymeric structure from aqueous molecular dynamics simulations of oligosaccharides: predictions from simulations of hyaluronan tetrasaccharides compared with hydrodynamic and x-ray fiber diffraction data
AUTHOR(S): Almond, A.; Brass, A.; Sheehan, J. K.
CORPORATE SOURCE: Division of Biochemistry School of Biological Sciences, University of Manchester, Manchester, M13 9PT, UK
SOURCE: Journal of Molecular Biology (1998), 284(5), 1425-1437
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mol. dynamics simulations of the two hyaluronan tetrasaccharides in water predict that over a period of 500 ps, their central linkages populate a single primary min. Over the same period the peripheral linkages explore this min., but also a secondary min. Structures constructed using the primary min. were found to be extended left-handed helixes of axial rise per disaccharide (h) 0.8 to 1.0 nm and 2.8 to 4.5 disaccharides per turn (n), in good agreement with n = 3 and n = 4 helixes found by x-ray fiber diffraction studies. We have used the predicted av. conformation from mol. dynamics to calc. the translational diffusion coeffs. of the oligosaccharide series up to decasaccharide, and compared these with exptl. measurements obtained using the method of capillary dispersion. Our calcd. values are found to be in good agreement with expt. beyond the size of a tetrasaccharide. A partial digest of hyaluronan in the mol. mass range 10 to 100 kDa was fractionated by gel chromatog. Mol. wts. were detd. by in-line laser light-scattering measurements, and the translational diffusion coeffs. of selected fractions were detd. by dynamic laser light-scattering. A similar expt. was performed on hyaluronan with a mol. mass greater than 1 MDa. The data suggest a change from rod-like to stiff coil behavior beyond a mol. wt. of 10 kDa. We have also examd. the conformations available using the secondary min., found at the peripheral linkages. In contrast to the extended structures previously described we have found left and right-handed helixes with high values of n (5-10) and low values of h. Although there is no exptl. evidence for these structures, they are of interest as, over short stretches, they would introduce folds, loops, and turns into the hyaluronan mol. Such shapes may play an important role in the hydrodynamics of hyaluronan and its interaction with lipids and proteins. (c) 1998 Academic Press.

IT **216065-16-6**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(mol. dynamics of)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:798976 HCAPLUS
DOCUMENT NUMBER: 130:150126
TITLE: Structure determination for octasaccharides derived from the carbohydrate-protein linkage region of chondroitin sulfate chains in the proteoglycan aggrecan from bovine articular cartilage
AUTHOR(S): Huckerby, Thomas N.; Lauder, Robert M.; Nieduszynski, Ian A.
CORPORATE SOURCE: The Polymer Centre, School of Physics and Chemistry, Lancaster University, Lancaster, LA1 4YA, UK
SOURCE: European Journal of Biochemistry (1998), 258(2), 669-676
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Five octasaccharides derived from the protein carbohydrate linkage region of chondroitin sulfate (CS) have been isolated from the large aggregating proteoglycan (aggrecan) extd. from the bovine articular cartilage of 6-yr-old to 8-yr-old animals. Following the purifn. of aggrecan the attached CS chains were digested with CS ABC endolyase and subsequently released from the protein core by .beta.-elimination. The individual oligosaccharides were purified by strong anion-exchange chromatog. and their structures detd. by very high-field one-dimensional and two-dimensional 1H-NMR spectroscopy. They were found to be octasaccharides, comprised of tetrasaccharide repeat-region extensions to the core tetrasaccharide linkage region structure. They have the following structures:.DELTA.UA(.beta.1-3)GalNAc(.beta.1-4)GlcA(.beta.1-3)GalNAc(.beta.1-4)GlcA(.beta.1-3)Gal(.beta.1-3)Gal(.beta.1-4)Xyl-ol, .DELTA.UA(.beta.1-3)GalNAc(.beta.1-4)GlcA(.beta.1-3)GalNAc6S(.beta.1-4)GlcA(.beta.1-3)Gal(.beta.1-3)Gal(.beta.1-4)Xyl-ol, .DELTA.UA(.beta.1-3)GalNAc6S(.beta.1-4)GlcA(.beta.1-3)GalNAc(.beta.1-4)GlcA(.beta.1-3)Gal(.beta.1-3)Gal(.beta.1-4)Xyl-ol, .DELTA.UA(.beta.1-3)GalNAc6S(.beta.1-4)GlcA(.beta.1-3)GalNAc6S(.beta.1-4)GlcA(.beta.1-3)Gal(.beta.1-3)Gal(.beta.1-4)Xyl-ol and .DELTA.UA(.beta.1-3)GalNAc4S(.beta.1-4)GlcA(.beta.1-3)GalNAc6S(.beta.1-4)GlcA(.beta.1-3)Gal(.beta.1-3)Gal(.beta.1-4)Xyl-ol. They differ only in the nature of the sulfation of the GalNAc residues of the tetrasaccharide-repeat-region extension, which forms the first two disaccharides of the repeat region. No sulfation of any of the uronic acid residues has been identified and in one oligosaccharide neither of the GalNAc residues were sulfated. The majority of the linkage regions contained GalNAc residues which were fully 6-sulfated. However, in a significant amt., only one of the residues was 6-sulfated while the other was either unsulfated or 4-sulfated. There was no evidence either for sulfation of the linkage region galactose residues or for phosphorylation of the xylose residue, through which the chain is attached to the core protein.

IT **220222-62-8**
RL: BOC (Biological occurrence); BPR (Biological process); BSU

(Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(structure detn. for octasaccharides derived from carbohydrate-protein linkage region of chondroitin sulfate chains in proteoglycan aggrecan from bovine articular cartilage)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:657768 HCAPLUS
DOCUMENT NUMBER: 130:14142
TITLE: Dynamic exchange between stabilized conformations predicted for hyaluronan tetrasaccharides: comparison of molecular dynamics simulations with available NMR data
AUTHOR(S): Almond, Andrew; Brass, Andy; Sheehan, John K.
CORPORATE SOURCE: Division of Biochemistry, School of Biological Sciences, University of Manchester, Manchester, M13 9PT, UK
SOURCE: Glycobiology (1998), 8(10), 973-980
CODEN: GLYCE3; ISSN: 0959-6658
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Studies of the hyaluronan (HA) tetrasaccharides are important for understanding hydrogen-bonding in the HA polymer, as they are probably the smallest oligomers in which characteristics of the constituent monosaccharides and the polymer are simultaneously exhibited. Here we present extensive mol. dynamics simulations of the two tetrasaccharides of HA in dil. aq. soln. These simulations have confirmed the existence of intramol. hydrogen-bonds between the neighboring sugar residues of HA in soln., as proposed by Scott (1989). However, our simulations predict that these intramol. hydrogen-bonds are not static as previously proposed, but are in const. dynamic exchange on the sub-nanosecond time-scale. This process results in discrete internal motion of the HA tetrasaccharides where they rapidly move between low energy conformations. Specific interactions between water and intramol. hydrogen-bonds involving the hydroxymethyl group were found to result in differing conformations and dynamics for the two alternative tetrasaccharides of HA. This new observation suggests that this residue may play a key role in the entropy and stability of HA in soln., allowing it to stay sol. up to high concn. The vicinal coupling consts. 3JNHCH of the acetamido groups have been calcd. from our aq. simulations of HA. We found that high values of 3JNHCH .apprxeq. 8 Hz, as exptl. measured for HA, are consistent with mixts. of both trans and cis conformations, and thus 3JNHCH cannot be used to imply a purely trans conformation of the acetamido. The rapid exchange of intramol. hydrogen-bonds indicates that although the structure is at any moment stabilized by these hydrogen-bonds, no one hydrogen-bond exists for an extended period of time. This could explain why NMR often fails to provide evidence for intramol. hydrogen-bonds in HA and other aq. carbohydrate structures.

IT **216065-16-6**
RL: PRP (Properties)
(dynamic exchange between stabilized conformations predicted for

hyaluronan tetrasaccharides and comparison of mol. dynamics simulations with available NMR data)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:567533 HCAPLUS
DOCUMENT NUMBER: 129:276150
TITLE: Synthesis of hyaluronic-acid-related oligosaccharides and analogs, as their 4-methoxyphenyl glycosides, having N-acetyl-.beta.-D-glucosamine at the reducing end
AUTHOR(S): Halkes, Koen M.; Slaghek, Ted M.; Hypponen, Teija K.; Kruiskamp, Peter H.; Ogawa, Tomoya; Kamerling, Johannis P.; Vliegenthart, Johannes F. G.
CORPORATE SOURCE: Bijvoet Center, Department of Bio-Organic Chemistry, Utrecht University, Utrecht, NL-3508 TB, Neth.
SOURCE: Carbohydrate Research (1998), 309(2), 161-174
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:276150
AB To study the ability of oligosaccharide fragments of hyaluronic acid to induce angiogenesis, several hyaluronic-acid-related oligosaccharides and their 6-O-sulfated analogs were synthesized as their 4-methoxyphenyl glycosides having 2-acetamido-2-deoxy-D-glucopyranose at the reducing end. In all syntheses described, the D-glucopyranosyl-uronic acid residue was obtained by oxidn. at C-6 of a corresponding D-glucopyranosyl residue after construction of the oligosaccharide backbone, using pyridinium dichromate and acetic anhydride.
IT **213899-51-5P 213899-52-6P 213899-53-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of hyaluronic-acid-related oligosaccharides and analogs, as their 4-methoxyphenyl glycosides, having N-acetyl-.beta.-D-glucosamine at the reducing end)

L8 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:534525 HCAPLUS
DOCUMENT NUMBER: 129:258636
TITLE: .alpha.-N-Acetylgalactosamine-capping of chondroitin sulfate core region oligosaccharides primed on xylosides
AUTHOR(S): Miura, Yoshiaki; Freeze, Hudson H.
CORPORATE SOURCE: Burnham Institute, La Jolla, CA, 92037, USA
SOURCE: Glycobiology (1998), 8(8), 813-819
CODEN: GLYCE3; ISSN: 0959-6658
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors previously reported that cultured mammalian cells

incubated with 4-methylumbelliferyl (MU) or p-nitrophenyl (pNP) .beta.-xyloside synthesize an .alpha.-GalNAc-terminated pentasaccharide resembling the glycosaminoglycan-core protein linkage region. Here the authors show that human melanoma M21 cells and human neuroblastoma cells incubated with Xyl.beta.-MU/pNP also make an .alpha.-GalNAc-terminated heptasaccharide contg. one chondroitin disaccharide repeat. High performance liq. chromatog. and matrix-assisted laser desorption ionization mass spectrometry anal. of intact or glycosidase-digested xyloside showed the structure as: GalNAc.alpha.GlcA-.beta.1,3GalNAc.beta.1,4GlcA.beta.1, 3Gal.beta.1,3Gal.beta.1,4Xyl.beta.-MU/pNP. The .alpha.-GalNAc-terminated xylosides can account for .apprx.10% of the total Xyl.beta.-MU/pNP products (.apprx.1.5 nmol/h/mg). These results show that GalNAc.alpha.GlcA.beta.-modification is relatively abundant, but not unique to the GAG-linkage tetrasaccharide. .alpha.-GalNAc addn. to the GlcA residue does not appear to be an extension of general phase II detoxification of xenobiotics that involve glucuronidation, since M21 cells incubated with MU synthesize only 0.3 pmol GlcA.beta.-MU/h/mg protein, and undetectable amt. of GalNAc.alpha.GlcA.beta.-MU (<40 fmol/h/mg). Further, subcellular fractionation shows that the .alpha.-N-acetylgalactosaminyltransferase activity colocalizes in the Golgi with other glycosyl transferases and not in the ER, where xenobiotic detoxification glucuronosyltranferases are found. Although GalNAc.alpha.GlcA.beta.-terminal modification has not been detected on naturally occurring GAG chains, the substantial amt. of .alpha.-GalNAc transferase activity suggests that the .alpha.-GalNAc transferase could utilize other GlcA-contg. glycoconjugates as acceptors.

IT **213611-50-8**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(.alpha.-N-Acetylgalactosamine-capping of chondroitin sulfate core region oligosaccharides primed on xylosides in human cancer cells)

L8 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:706972 HCAPLUS
DOCUMENT NUMBER: 128:45120
TITLE: Characterization of serum .beta.-glucuronyltransferase involved in chondroitin sulfate biosynthesis
AUTHOR(S): Kitagawa, Hiroshi; Ujikawa, Miho; Tsutsumi, Kae; Tamura, Jun-Ichi; Neumann, Klaus W.; Ogawa, Tomoya; Sugahara, Kazuyuki
CORPORATE SOURCE: Department of Biochemistry, Kobe Pharmaceutical University, Kobe, 658, Japan
SOURCE: Glycobiology (1997), 7(7), 905-911
CODEN: GLYCE3; ISSN: 0959-6658
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We studied a glucuronyltransferase involved in chondroitin sulfate (CS) biosynthesis in a prepn. obtained from fetal bovine serum by heparin-Sepharose affinity chromatog. This enzyme transferred GlcA from UDP-GlcA to the nonreducing GalNAc residues of polymeric

chondroitin. It required Mn2+ for maximal activity and showed a sharp pH optimum between pH 5.5 and 6.0. The apparent Km value of the glucuronyltransferase for UDP-GlcA was 51 .mu.M. The specificity was investigated using structurally defined acceptor substrates, which consisted of chem. synthesized tri-, penta-, and heptasaccharide-serines and various odd-numbered oligosaccharides with a GalNAc residue at the nonreducing terminus, prepd. from chondroitin and CS by chondroitinase ABC digestion followed by mercuric acetate treatment. The enzyme utilized a heptasaccharide-serine GalNAc.beta.1-4GlcA.beta.1-3GalNAc.beta.1-4GlcA.beta.1-3Gal.beta.1-3Gal.beta.1-4Xyl.beta.1-O-Ser and a pentasaccharide-serine GalNAc.beta.1-4GlcA.beta.1-3Gal.beta.1-3Gal.beta.1-4Xyl.beta.1-O-Ser as acceptors. In contrast, neither a trisaccharide-serine Gal.beta.1-3Gal.beta.1-4Xyl.beta.1-O-Ser nor an .alpha.-GalNAc-capped pentasaccharide-serine GalNAc.alpha.1-4GlcA.beta.1-3Gal.beta.1-3Gal.beta.1-4Xyl.beta.1-O-Ser that is a model compd. of the reaction product formed by the action of the .alpha.-GalNAc transferase recently demonstrated in fetal bovine serum (Kitagawa et al., J. Biol. Chem., 270, 22190-22195, 1995) was utilized as an acceptor. Besides, all nonsulfated odd-numbered oligosaccharides except for the trisaccharide GalNAc.beta.1-4GlcA.beta.1-3GalNAc served as acceptors and the transfer rates roughly increased with increasing chain length. Moreover, 6-O-sulfation of nonreducing terminal GalNAc markedly enhanced GlcA transfer, whereas 4-O-sulfation had little effect on it. These results indicated that at least two glucuronyltransferases are involved in the biosynthesis of CS and that sulfation reactions may play important roles in chain elongation.

IT **199943-20-9 199943-21-0 199943-22-1**
199943-23-2 199943-24-3 200053-51-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(characterization of serum .beta.-glucuronyltransferase involved in chondroitin sulfate biosynthesis)

L8 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:697710 HCAPLUS
DOCUMENT NUMBER: 127:346590
TITLE: Isolation and characterization by electrospray-ionization mass spectrometry and high-performance anion-exchange chromatography of oligosaccharides derived from hyaluronic acid by hyaluronate lyase digestion: observation of some heretofore unobserved oligosaccharides that contain an odd number of units
AUTHOR(S): Price, Kenneth N.; Tuinman, Al; Baker, David C.; Chisena, Christina; Cysyk, Richard L.
CORPORATE SOURCE: Department of Chemistry, University of Tennessee, Knoxville, TN, 37996, USA
SOURCE: Carbohydrate Research (1997), 303(3), 303-311
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hyaluronic acid was degraded with hyaluronate lyase (E.C. 4.2.2.1, from Streptomyces hyalurolyticus), and the resulting oligosaccharides up to dp 16 were characterized by electrospray-ionization mass spectrometry (ESIMS) and

high-performance anion-exchange chromatog. (HPAEC) with pulsed amperometric detection (PAD). In accordance with the known regiospecificity of the enzyme, the products included even-numbered oligosaccharides of structure .alpha.-L-4en-thrHexpA-(1.fwdarw.3)-[.beta.-D-GlcpNAc-(1.fwdarw.4)-.beta.-D-GlcpA]n-(1.fwdarw.3)-D-GlcpNAc. Minor amts. of novel and unexpected odd-numbered oligomers, having the structure .alpha.-L-4en-thrHexpA-(1.fwdarw.3)-[.beta.-D-GlcpNAc-(1.fwdarw.4)-D-GlcpA]n, were also isolated and characterized. This study, in addn. to others beginning to appear in the literature, demonstrates the usefulness of ESIMS and HPAEC-PAD in the anal. and characterization of anionic glycosaminoglycan-type oligosaccharides.

IT **198191-91-2P 198191-92-3P 198191-93-4P**
198191-94-5P 198191-95-6P 198191-96-7P
198191-97-8P 198191-98-9P 198191-99-0P
198192-00-6P
RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(isolation and mol. structure of oligosaccharides derived from hyaluronic acid by hyaluronate lyase digestion using mass spectrometry and high performance anion exchange chromatog.)

L8 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:386338 HCAPLUS
DOCUMENT NUMBER: 127:118872
TITLE: Regulation of chondroitin sulfate biosynthesis by specific sulfation: acceptor specificity of serum .beta.-GalNAc transferase revealed by structurally defined oligosaccharides
AUTHOR(S): Kitagawa, Hiroshi; Tsutsumi, Kae; Ujikawa, Miho; Goto, Fumitaka; Tamura, Jun-ichi; Neumann, Klaus W.; Ogawa, Tomoya; Sugahara, Kazuyuki
CORPORATE SOURCE: Department of Biochemistry, Kobe Pharmaceutical University, Kobe, 658, Japan
SOURCE: Glycobiology (1997), 7(4), 531-537
CODEN: GLYCE3; ISSN: 0959-6658
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The relationship between sulfation and polymn. in chondroitin sulfate (CS) biosynthesis has been poorly understood. In this study, we investigated the specificity of bovine serum UDP-GalNAc:CS .beta.-GalNAc transferase responsible for chain elongation using structurally defined acceptor substrates. They consisted of tetra- and hexasaccharide-serines that were chem. synthesized and various regular oligosaccharides with a GlcA residue at the nonreducing terminus, prepd. from chondroitin and CS using testicular hyaluronidase. The enzyme prepn. was obtained from fetal bovine serum by mans of heparin-Sepharose affinity chromatog. The prepn. did not contain the .alpha.-GalNAc transferase recently demonstrated in fetal bovine serum (Kitagawa et al., J. Biol. Chem., 270, 22190-22195, 1995), that utilizes common acceptor substrates. The .beta.-GalNAc transferase used as acceptors, two hexasaccharide-serines GlcA.beta.1-3GalNAc.beta.1-4GlcA.beta.1-3Gal.beta.1-3Gal.beta.1-4Xyl.beta.1-O-Ser and GlcA.beta.1-3GalNAc(4-sulfate).beta.1-4GlcA.beta.1-3Gal(4-sulfate).beta.1-3Gal.beta.1-4Xyl.beta.1-O-Ser, but neither the monosulfated hexasaccharide-serine GlcA.beta.1-3GalNAc(4-sulfate).beta.1-4Glc-A.beta.1-

3Gal.beta.1-3Gal.beta.1-4xyl.beta.1-O-Ser, nor tetrasaccharide-serines with or without a sulfate group at C-4 of the third su residue Gal-3 from the reducing end. The results indicated th sulfate group at the Gal-3 C-4 markedly affected the transfer GalNAc to the terminal GlcA. In addn., a sulfate group at C-4 of the reducing terminal GalNAc of regular tetrasaccharides remarkably enhanced the GalNAc transfer, suggesting that the enzyme recognizes up to the fourth saccharide residue from the nonreducing end. The level of incorporation into a tetra- or hexasaccharide contg. a terminal 2-O-sulfated GlcA residue was significant, whereas there was no apparent incorporation into tetra- or hexasaccharides contg. a terminal 3-O-sulfated GlcA or penultimate 4,6-O-disulfated GalNAc residue. These results indicated that sulfation reactions play important roles in chain elongation and termination.

IT **73603-40-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(model substrate; regulation of chondroitin sulfate biosynthesis by specific sulfation and acceptor specificity of serum .beta.-GalNAc transferase revealed by structurally defined oligosaccharides)

L8 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:258871 HCAPLUS
DOCUMENT NUMBER: 123:170004
TITLE: Synthesis of hyaluronic acid related di- and tetrasaccharides having a glucuronic acid at the reducing end
AUTHOR(S): Slaghek, Ted M.; Hypponen, Teija K.; Ogawa, Tomoya; Kamerling, Johannis P.; Vliegenthart, Johannes F. G.
CORPORATE SOURCE: Dep. of Bio-Organic Chem., Utrecht Univ., Utrecht, NL-2508 TB, Neth.
SOURCE: Tetrahedron: Asymmetry (1994), 5(11), 2291-301
CODEN: TASYE3; ISSN: 0957-4166
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 4-Methoxyphenyl O-2-acetamido-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosiduronic acid (I) and 4-methoxyphenyl O-2-acetamido-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-acetamido-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-.beta.-D-glucopyranosiduronic acid (II), which represent structural elements of hyaluronic acid, were prepd. 3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-.beta.-D-glucopyranosyl trichloroacetimidate was condensed with 4-methoxyphenyl 6-O-levulinoyl-2,3-di-O-p-toluoyl-.beta.-D-glucopyranoside (III) to give the expected .beta.-(1.fwdarw.4)-linked disaccharide (IV). Subsequent delevulinoylation, oxidn., complete deprotection, and N-acetylation gave I. Coupling of 3-O-allyloxycarbonyl-2-deoxy-4,6-O-isopropylidene-2-phthalimido-.beta.-D-glucopyranosyl trichloroacetimidate with III, followed by de-allyloxycarbonylation of the obtained disaccharide deriv. gave 4-methoxyphenyl O-2-deoxy-4,6-O-isopropylidene-2-phthalimido-.beta.-D-glucopyranosyl-(1.fwdarw.4)-6-O-levulinoyl-2,3-di-O-p-toluoyl-.beta.-D-glucopyranoside (V). Demethoxyphenylation and subsequent imidation of IV afforded O-3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-.beta.-D-glucopyranosyl-(1.fwdarw.4)-6-O-levulinoyl-2,3-di-O-p-toluoyl-

.alpha./.beta.-D-glucopyranosyl trichloroacetimidate (VI). Condensation of V with VI, followed by deisopropylidenation, O-acetylation, delevulinoylation, oxidn., complete deprotection, and N-acetylation of the obtained tetrasaccharide deriv. gave II.

IT **153984-85-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of hyaluronic acid-related di- and tetrasaccharides having glucuronic acid at the reducing end)

L8 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:218359 HCAPLUS
DOCUMENT NUMBER: 120:218359
TITLE: Synthesis of a tetrasaccharide fragment of hyaluronic acid having a glucuronic acid at the reducing end. Part 3
AUTHOR(S): Slaghek, Ted M.; Hyppoenen, Teija K.; Ogawa, Tomoya; Kamerling, Johannis P.; Vliegenthart, F. G.
CORPORATE SOURCE: Bijvoet Cent., Utrecht Univ., Utrecht, 3508 TB, Neth.
SOURCE: Tetrahedron Lett. (1993), 34(49), 7939-42
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:218359
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A stereocontrolled synthesis of a tetrasaccharide fragment of hyaluronic acid, .beta.-p-methoxyphenyl glycoside of .beta.-D-GlcNAc-(1.fwdarw.4)-.beta.-D-GlcA-(1.fwdarw.3)-.beta.-D-GlcNAc-(1.fwdarw.4)-D-GlcA, was carried out in a highly stereoselective glycosidation reaction by using one monosaccharide acceptor I and two monosaccharide donors II and III.

IT **153984-85-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate in prepn. of a tetrasaccharide fragment of hyaluronic acid having a glucuronic acid at the reducing end)

L8 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:536299 HCAPLUS
DOCUMENT NUMBER: 119:136299
TITLE: Effects of exogenous hyaluronic acid and serum on matrix organization and stability in the mouse cumulus cell-oocyte complex
AUTHOR(S): Camaioni, Antonella; Hascall, Vincent C.; Yanagishita, Masaki; Salustri, Antonietta
CORPORATE SOURCE: Bone Res. Branch, Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA
SOURCE: J. Biol. Chem. (1993), 268(27), 20473-81
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Compact cumulus cell-oocyte complexes (COCs) isolated from

preovulatory mouse follicles undergo expansion in vitro when high levels of hyaluronic acid (HA) are synthesized and organized into an extracellular matrix. The authors studied the effects of fetal bovine serum (FBS) and of exogenous HA and HA-oligomers on the expansion process. Max. retention of HA in the COC matrix, and hence complete COC expansion, occurs when 1% FBS is continuously present during the 1st 18 h of culture. Irresp. of the culture time, HA synthesized when serum is absent is primarily in the medium, whereas HA synthesized when serum is present is primarily in the cell matrix. These findings support the hypothesis that the serum factor, identified as an inter-.alpha.-trypsin inhibitor by L. Chen et al. (1992), is a structural component of the matrix. Addn. of exogenous HA or of HA oligomers of decasaccharide size (GlcUA-GlcNAc)5 or larger effectively displaces endogenously synthesized HA from the matrix into the medium, thereby preventing COC expansion. Addn. of exogenous chondroitin sulfate affects neither matrix organization nor COC expansion, thus indicating specificity of the binding of some structural component(s) to HA. Fully expanded COCs disassemble when cultured >18 h, a process which occurs also in vivo and which correlates with loss of oocyte fertilizability both in vivo and in vitro. This process involves release of macromol. HA from the matrix into the medium, with loss of 50% of the HA in the 1st 8 h of incubation after full expansion. The release is not facilitated when HA oligomers, long enough to prevent matrix formation, are added to the culture medium after the COCs are fully expanded. This suggests that cooperative binding to HA of either the serum factor, an endogenously synthesized factor(s), or both is required to stabilize the fully expanded COC matrix.

IT **57282-62-9**
RL: BIOL (Biological study)
(extracellular matrix organization and stability in cumulus cell-oocyte complex response to, blood serum effect on)

L8 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:204455 HCAPLUS
DOCUMENT NUMBER: 112:204455
TITLE: Skin-lightening, moisturizing, and sunscreening cosmetics containing hyaluronic acid hydrolyzates
INVENTOR(S): Honda, Goro
PATENT ASSIGNEE(S): Tokyo Sankei Kagaku Y. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01272511	A2	19891031	JP 1988-98798	19880421

AB Skin-lightening, moisturizing, and sunscreening cosmetics contain (i) tetrasaccharide, disaccharide, hexasaccharide, and/or deoxydisaccharide prepd. by treatment of hyaluronic acid (salts) with testicular or bacterial hyaluronidase or (ii) ring-cleavaged disaccharides. The oligosaccharides have good moisturizing, tyrosinase-inhibiting, and UV-absorbing effects, show good

storage-stability, and give no side effects. A hair prepn. comprised EtOH 55.0, purified castor oil 10.0, salicylic acid 0.3, surfactant 1.0, oligosaccharides 2.0, perfume, colorant, and H2O to 100%.

IT **57323-42-9P**
RL: PREP (Preparation)
(prepn. of, for skin-lightening and moisturizing and sunscreening cosmetics)

L8 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:144401 HCAPLUS
DOCUMENT NUMBER: 104:144401
TITLE: Purification and characterization of a 3'-phosphoadenylylsulfate:chondroitin 6-sulfotransferase from arterial tissue
AUTHOR(S): Hollmann, Juergen; Niemann, Reinhard; Buddecke, Eckhart
CORPORATE SOURCE: Inst. Physiol. Chem., Univ. Muenster, Muenster, D-4400, Fed. Rep. Ger.
SOURCE: Biol. Chem. Hoppe-Seyler (1986), 367(1), 5-13
CODEN: BCHSEI
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A 3'-phosphoadenylylsulfate:chondroitin sulfotransferase (EC 2.8.2.5) was purified to homogeneity (.apprx.760-fold) from the cytosolic fraction of calf arterial tissue by Con A-Sepharose, ion-exchange, and affinity chromatog. The enzyme has a mol. mass of 38,000 daltons, optimal activity at pH 6.0 (100%) and 7.25 (75%), requires divalent cations for max. activity (Mn2+ .gtoreq. Mg2+, Ca2+), and exhibits specificity towards desulfated chondroitin sulfate and oligosaccharides derived therefrom. The enzyme transfers sulfate groups from [35S]phosphoadenylylsulfate exclusively to C-6 OH groups of N-acetylgalactosamine units of the acceptor substrates. Max. sulfate transfer occurs at 2 mM chondroitin disaccharide units (100%), the transfer rates decreasing with decreasing chain length in the order deca- (55%), octa- (17%), and hexasaccharides (4%). Lineweaver-Burk plots revealed equal max. velocities for chondroitin and deca-, octa-, and hexasaccharides, but decreasing Km values. Chondroitin 4-sulfate has 21% of the acceptor potency exhibited by chondroitin, whereas dermatan sulfate, heparan sulfate, hyaluronate, and the chondroitin tetrasaccharide showed no acceptor properties. Anal. of the reaction products formed by prolonged enzymic sulfation of a reduced chondroitin hexasaccharide [GlcA-GalNAc]2-GlcA-GalNAc-ol revealed that the preterminal N-acetylgalactosamine from the nonreducing end and the internal N-acetylgalactosamine, but not the N-acetylgalactosaminitol, were sulfated and that no hexasaccharide disulfate was formed by the action of chondroitin 6-sulfotransferase. Chondroitin 6-sulfotransferase is considered to possess a binding region capable of accommodating a nonsulfated oligosaccharide sequence of .gtoreq.6 sugars and is believed to act in the course of chondroitin sulfate synthesis in cooperation with, but shortly after, the enzymes involved in the chain elongation reaction.

IT **73603-40-4 101205-01-0 101312-53-2 101312-54-3**
RL: RCT (Reactant)
(reaction of, with chondroitin 6-sulfotransferase of artery,

kinetics of)

L8 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:484358 HCAPLUS
DOCUMENT NUMBER: 103:84358
TITLE: Comparison of relationships between the chemical structures and mobilities of hyaluronate oligosaccharides in thin-layer and high-performance liquid chromatography
AUTHOR(S): Shimada, Eiji; Matsumura, Go
CORPORATE SOURCE: Sch. Pharm. Sci., Showa Univ., Tokyo, 142, Japan
SOURCE: J. Chromatogr. (1985), 328, 73-80
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Rm {log[(1/RF)-1]} values of odd- and even-numbered hyaluronate oligosaccharides comprised of N-acetylglucosamine and glucuronic acid residues were detd. by TLC. Previous retention time data of the acidic oligosaccharides obtained by HPLC were converted into Rm values. By dividing the oligosaccharide structures into several fragments, the contributions of these fragments to chromatog. mobility (group consts.) were estd. essentially from the difference between the Rm values of 2 oligomers having appropriate structures. The group consts. of the bridging O atoms at the .beta.-1,4- and -1,3-glycosidic linkages of these oligomers were identical in HPLC but not in TLC. In the 2 types of chromatog., the mobility of a given hyaluronate oligosaccharide could be explained by a linear combination of group consts. and the Rm value of N-acetylglucosamine or glucuronic acid, with the exception that the Rm value of the uronic acid in TLC was anomalous.
IT **57282-67-4 57323-42-9 57323-43-0 85425-43-0 87142-75-4**
RL: ANST (Analytical study)
(chromatog. mobility of, in thin-layer and high-performance liq. chromatog.)

L8 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:483726 HCAPLUS
DOCUMENT NUMBER: 103:83726
TITLE: Interaction of hyaluronectin with hyaluronic acid oligosaccharides
AUTHOR(S): Bertrand, Philippe; Delpech, Bertrand
CORPORATE SOURCE: Lab. Immunochim., Cent. Henri Becquerel, Rouen, 76000, Fr.
SOURCE: J. Neurochem. (1985), 45(2), 434-9
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hyaluronic acid was digested by bovine testicular hyaluronidase, and oligomers were fractionated by gel permeation using AcA 202 Ultrogel, an acrylamide-agarose matrix. Oligosaccharides composed of 2-6 disaccharide repeating units were isolated. Two nonasaccharides were prepd. by enzymic or chem. modification of the decasaccharide. Oligosaccharides were compared (by competitive inhibition of the ELISA for their ability to inhibit the interaction of hyaluronectin (a hyaluronic acid-binding brain glycoprotein) with hyaluronic acid. Among these oligosaccharides, decasaccharides were the smallest fragments that strongly inhibited the interaction.

Octasaccharides inhibited with 700-fold lower affinity than desasaccharides. Dodecascaccharides had the same effect as decasaccharides. Nonasaccharides obtained by .beta.-glucuronidase splitting of decasaccharides inhibited the interaction more than nonasaccharides prepd. by alk. treatment.

IT **57282-62-9 57323-42-9 57323-43-0 71058-12-3 71058-13-4 71058-16-7**
RL: BIOL (Biological study)
(hyaluronectin of brain interaction with)

L8 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:200533 HCAPLUS
DOCUMENT NUMBER: 102:200533
TITLE: Comparison of gel permeation and ion-exchange chromatographic procedures for the separation of hyaluronate oligosaccharides
AUTHOR(S): Nebinger, Peter
CORPORATE SOURCE: Fachber. Biol. Chem., Univ. Osnabrueck, Osnabrueck, D-4500, Fed. Rep. Ger.
SOURCE: J. Chromatogr. (1985), 320(2), 351-9
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB For the sepn. of hyaluronate oligosaccharides, gel permeation chromatog. on Sephadex G-25 and ion-exchange chromatog. on Dowex 1-X8 (formate form), DEAE Sephacel (chloride, acetate and formate forms) and Trisacryl M (acetate and formate forms) were compared. Best results were obtained from DEAE Sephacel (formate form) and Dowex 1-X8 (formate form). Even- and odd-numbered hyaluronic acid oligosaccharides up to decasaccharide were well sepd. Contaminations were detected by HPLC.

IT **57282-67-4 57323-42-9 57323-43-0 85425-43-0 87142-75-4 87147-49-7 96359-36-3**
RL: ANT (Analyte); ANST (Analytical study)
(chromatog. of, gel and ion-exchange, comparison of, of hyaluronate)

L8 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:145088 HCAPLUS
DOCUMENT NUMBER: 102:145088
TITLE: The application of the Milner-Avigad method for the quantitative determination of endouronidase activities
AUTHOR(S): Majima, Mitsuo; Takagaki, Keiichi; Igarashi, Seiko; Nakamura, Toshiya; Endo, Masahiko
CORPORATE SOURCE: Sch. Med., Hirosaki Univ., Hirosaki, 036, Japan
SOURCE: J. Biochem. Biophys. Methods (1984), 10(3-4), 143-51
CODEN: JBBMDG; ISSN: 0165-022X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The method of Y. Milner and G. Avigad (1967) was applied to the quant. detn. of endouronidase activity. Among the constituent monosaccharides of glycosaminoglycans, hexuronic acids showed high color yield by this method, whereas xylose, galactose, and N-acetylhexosamine recorded negligible color yield. Among the monosaccharide residues at the reducing terminals of

oligosaccharides, only hexuronic acids exhibited color yield. However, the color yield was less than that of free hexuronic acids. Gel filtration chromatog. of reaction products revealed that the cleavage of the oligosaccharide chains and the resultant exposure of new reducing terminals were not caused by the reaction procedures involved in this method. These data indicate that the Milner-Avigad method is useful for detg. the presence of hexuronic acid residues preferentially at reducing terminals of glycosaminoglycan moieties. Thus, it supported the conclusion that the Milner-Avigad method is applicable for the quant. detn. of endouronidase activity with glycosaminoglycan as a substrate.

IT **57323-42-9**
RL: PRP (Properties)
(reducing power of, anal. by cupric ion redn. of, endouronidase detn. in relation to)

L8 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:43391 HCAPLUS
DOCUMENT NUMBER: 102:43391
TITLE: Studies in vitro on the uptake and degradation of sodium hyaluronate in rat liver endothelial cells
AUTHOR(S): Smedsroed, Baard; Pertoft, Haakan; Eriksson, Sigbritt; Fraser, J. Robert E.; Laurent, Torvard C.
CORPORATE SOURCE: Dep. Med. Chem., Univ. Uppsala, Uppsala, S-751 23, Swed.
SOURCE: Biochem. J. (1984), 223(3), 617-26
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Rat liver endothelial cells in primary cultures at 7.degree. bind radioactively labeled Na hyaluronate (HA; mol wt. 400,000) specifically and with high affinity (dissocn. const. = 6 .times. 10-11M). Max. binding capacity is .apprx.104 mols./cell. Inhibition expts. with unlabeled HA and oligosaccharides from HA indicate that each mol. is bound by several receptors acting cooperatively and that the single receptor recognizes a tetra- or hexasaccharide sequence of the polysaccharide. At 37.degree. the liver endothelial cells endocytose the HA. The process combines the features of a receptor-mediated and a fluid-phase endocytosis. The rate of internalization does not show any satn. with increasing HA concn., but is approx. proportional to the polysaccharide concn. at and above the physiol. concn. At 50 .mu.g free HA/L each liver endothelial cell accumulates 0.1 fg of the polysaccharide/min. Fluorescent HA accumulates in perinuclear granules, presumably lysosomes. Degrdn. products from HA appear in the medium .apprx.30 min after addn. of the polysaccharide to the cultures. The radioactivity from HA contg. N-[3H]acetyl groups or 14C in the sugar rings is recovered mainly as [3H]acetate and [14C]lactate, resp. Estns. of the capacity of liver endothelial cells to internalize and degrade HA in vitro indicate that these cells may be primarily responsible for the clearance of HA from human blood in vivo.

IT **57282-62-9 57323-42-9 57323-43-0**
93957-10-9 93957-11-0
RL: BIOL (Biological study)
(hyaluronate endocytosis and metab. by liver endothelial cells inhibition by)

L8 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:587205 HCAPLUS
DOCUMENT NUMBER: 101:187205
TITLE: Thin-layer chromatography of hyaluronate oligosaccharides
AUTHOR(S): Shimada, Eiji; Matsumura, Go
CORPORATE SOURCE: Sch. Pharm. Sci., Showa Univ., Tokyo, 142, Japan
SOURCE: J. Biochem. (Tokyo) (1984), 96(3), 721-5
CODEN: JOBIAO; ISSN: 0021-924X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Odd- and even-numbered hyaluronate oligosaccharides with N-acetylglucosamine, glucuronic acid, or 4,5-unsatd. glucuronic acid at their nonreducing ends were sepd. by TLC on silica gel with a solvent system of iso-PrOH-H2O (66:34) contg. 0.05M NaCl. In the iso-PrOH system, small amts. of electrolytes were necessary for the resoln. of each oligosaccharide.

IT **57282-67-4 71058-09-8 71086-83-4 85425-43-0 87142-75-4 92758-48-0 92758-49-1 92758-52-6 92758-53-7**
RL: ANST (Analytical study)
(sepn. of, by TLC, sodium chloride-contg. solvent system effect on)

L8 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:134615 HCAPLUS
DOCUMENT NUMBER: 100:134615
TITLE: Proton NMR of glycosaminoglycans and hyaluronic acid oligosaccharides in aqueous solution: the amide proton environment
AUTHOR(S): Cowman, Mary K.; Cozart, Dennis; Nakanishi, Koji; Balazs, Endre A.
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE: Arch. Biochem. Biophys. (1984), 230(1), 203-12
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The exchangeable amide protons of hyaluronic acid (HA) oligosaccharides and a higher-mol.-wt. segment dissolved in H2O at pH 2.5 or 5.5 were examd. by 1H NMR spectroscopy at 250 MHz. The HA segment prepn. showed a single amide resonance, near the chem. shift for the amide proton of the monosaccharide 2-acetamido-2-deoxy-.beta.-D-glucopyranose (.beta.-I). Smaller HA oligosaccharides showed 2 or 3 sep. amide proton resonances, corresponding in relative peak area to interior or end I residues. The interior I amide resonance occurred at the same chem. shift as the single resonance of the HA segment. For the end I residues, linkage to D-glucuronopyranose through C1 resulted in an upfield shift relative to the .beta.-anomer of I, whereas linkage through C3 resulted in a downfield shift relative to the corresponding anomer of I. These chem. shift perturbations appeared to be approx. offsetting in the case of linkage at both positions. The amide proton vicinal coupling const. (.apprx.9 Hz) was essentially independent of chain length, residue position, or soln. pH. These data favor a nearly perpendicular orientation for the acetamido group with respect to the sugar ring, little affected by linkage of I to

D-glucuronopyranose. No evidence for the existence of a stable H bond linking the amide proton with the carboxyl(ate) O of the adjacent uronic acid residue was found. The amide protein resonances for chondroitin, chondroitin 4-sulfate, and dermatan sulfate were compared to that of HA. The chem. shifts of these resonances deviated .ltoreq.0.1 ppm from that of HA. A small dependence on the identity of the adjacent uronic acid residues was noted, based on the observation of 2 resonances for dermatan sulfate.

IT **57323-42-9 71060-23-6 71177-54-3 85425-43-0**
RL: PRP (Properties)
(NMR of, of hyaluronic acid, pH effect on)

L8 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:518642 HCAPLUS
DOCUMENT NUMBER: 99:118642
TITLE: High-performance liquid chromatographic analysis of even- and odd-numbered hyaluronate oligosaccharides
AUTHOR(S): Nebinger, Peter; Koel, Marlies; Franz, Alfred; Werries, Eckhard
CORPORATE SOURCE: Fachber. Biol. Chem., Univ. Osnabrueck, Osnabrueck, D-4500, Fed. Rep. Ger.
SOURCE: J. Chromatogr. (1983), 265(1), 19-25
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Even-numbered oligosaccharides derived from hyaluronate which contain glucuronic acid or N-acetylglucosamine in a nonreducing position, as well as the corresponding odd-numbered oligosaccharides with N-acetylglucosamine or glucuronic acid at the nonreducing terminus, were sepd. by high-performance liq. chromatog. and identified at 206 nm. Using an amino-modified silica gel column and 0.1M KH2PO4 (pH 4.75) as the mobile phase, complete sepn. up to the octasaccharides was performed within 21 min. The effects of using various concns. of MeCN in the eluent and of using various pH values on the sepn. and retention data of the oligosaccharides were studied in detail.

IT **57282-67-4 57323-42-9 57323-43-0 71177-54-3 85425-43-0 87142-75-4 87147-49-7**
RL: PROC (Process)
(sepn. of, from hyaluronic acid by high-performance liq. chromatog.)

L8 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:501220 HCAPLUS
DOCUMENT NUMBER: 99:101220
TITLE: Hydrogen-bonded conformation of hyaluronate oligosaccharide fragments in aqueous solution
AUTHOR(S): Oberholtzer, J. C.; Englander, S. W.; Horwitz, A. F.
CORPORATE SOURCE: Sch. Med., Univ. Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: FEBS Lett. (1983), 158(2), 305-9
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The H bonding in hyaluronate oligosaccharide fragments was studied in aq. soln. with H-tritium exchange techniques. The data reveal an acetamido H exchange rate that is 5-6-fold slower than that seen in model compds. The magnitude of the slowing is interpreted as reflecting the participation of an acetamido H in a relatively labile intramol. H bond.

IT **57323-42-9 57323-43-0**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(hydrogen bonding in, hydrogen-tritium exchange in relation to)

L8 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:156891 HCAPLUS
DOCUMENT NUMBER: 98:156891
TITLE: Degradation of biogenic oligosaccharides by .beta.-N-acetylglucosaminidase secreted by Entamoeba histolytica
AUTHOR(S): Werries, Eckhard; Nebinger, Peter; Franz, Alfred
CORPORATE SOURCE: Biochem. Lab., Univ. Osnabrueck, Osnabrueck, D-4500, Fed. Rep. Ger.
SOURCE: Mol. Biochem. Parasitol. (1983), 7(2), 127-40
CODEN: MBIPDP; ISSN: 0166-6851
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .beta.-N-Acetylglucosaminidase secreted by E. histolytica was extd. from the growth medium by affinity chromatog. on CH-Sepharose 4B coupled to p-aminophenyl-1-thio-.beta.-2-acetamido-2-deoxyglucopyranoside. The enzyme was further purified by isoelec. focusing, by sequential chromatog. on DEAE-cellulose and Sephadex G-150, and by preparative disc gel electrophoresis. Chitobiose derived from chitin as well as a tri-, and tetra-, and a hexasaccharide derived from hyaluronic acid were tested as potential physiol. substrates. All these oligosaccharides are susceptible to action of .beta.-N-acetylglucosaminidase from E. histolytica. Under identical conditions chitobiose is cleaved 38-48 times faster than hyaluronate oligosaccharides. No release of N-acetylglucosamine was obsd. when glycopeptides from ovalbumin were used as substrates. The pH optimum of hydrolase activity was 4.5 when chitobiose was used as substrate. Optimal hydrolysis of hyaluronate oligosaccharides was obsd. at pH 3.0 for trisaccharide and pH 2.0 for tetra- and hexasaccharide, resp. Estn. of mol. wt. by gel filtration gave values of 75,000. The isoelec. point was 5.02. .beta.-N-Acetylglucosaminidase from E. histolytica does not act on macromol. chitin and hyaluronic acid.

IT **85425-43-0**
RL: RCT (Reactant)
(reaction of, with .beta.-N-acetylglucosaminidase, kinetics of)

L8 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:506103 HCAPLUS
DOCUMENT NUMBER: 97:106103
TITLE: Substrate specificity and regulation of activity of rat liver .beta.-D-glucuronidase
AUTHOR(S): Niemann, Reinhard; Buddecke, Eckhart
CORPORATE SOURCE: Inst. Physiol. Chem., Univ. Muenster, Muenster, D-4400, Fed. Rep. Ger.
SOURCE: Hoppe-Seyler's Z. Physiol. Chem. (1982), 363(6),

591-8
CODEN: HSZPAZ; ISSN: 0018-4888
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Highly purified rat liver .beta.-D-glucuronidase (I) catalyzes the hydrolysis of natural and synthetic .beta.-D-glucuronides. At pH 4, a release of glucuronic acid from chondroitin sulfate tetrasaccharide (GlcA-GalNAc sulfate)2, hyaluronate tetrasaccharide (GlcA-GlcNAc)2, Me .beta.-D-glucuronyl-.alpha.-D-glucoside, and p-nitrophenyl .beta.-D-glucuronide proceeds at relative rates of 1.0:0.55:0.22:1.5. In the presence of 0.4M NaCl, optimum hydrolysis shifts to pH 5.2 for the synthetic substrates, but natural substrates are not hydrolyzed under these conditions. .beta.-D-Glucuronyl saccharides bearing nonsulfated N-acetylhexosamine residue in preterminal position (disaccharides) are not hydrolyzed by I unless an addnl. glucuronic residue occupies the last but 2 position of the substrate (trisaccharide). Sulfation of the internal N-acetylhexosamine residue(s) enhances the rate of hydrolysis. In contrast to the nonhydrolyzable .beta.-D-glucuronyl-N-acetylglucosamine (hyaluronate disaccharide), .beta.-D-glucuronyl-anhydromannitol and Me .beta.-D-glucuronyl-.alpha.-D-glucoside are substrates for I. Hyaluronate and chondroitin sulfate trisaccharides with terminal nonreducing N-acetylhexosamine residues, are inhibitors of I. A regulatory function of chondroitin sulfate and hyaluronate derived odd-numbered oligosaccharides on the activity of .beta.-I under physiol. conditions is considered.

IT **57323-43-0**
RL: BIOL (Biological study)
(.beta.-glucuronidase specificity for)

L8 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:193429 HCAPLUS
DOCUMENT NUMBER: 92:193429
TITLE: Multiple kinetic forms of .beta.-glucuronidase
AUTHOR(S): Glaser, Janet H.; Conrad, H. Edward
CORPORATE SOURCE: Dep. Biochem., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: J. Biol. Chem. (1980), 255(5), 1879-84
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Partially purified chick embryo liver .beta.-glucuronidase and highly purified .beta.-glucuronidases from human placenta and rat preputial gland exhibit multiple kinetic forms which appear to exist in an equil. which is shifted by varying the assay conditions. All 3 enzymes exist in a low-Km form, which predominates at pH 3 and is stabilized by bovine serum albumin, and a high-Km form, which predominates at pH 5.5-6.0 in the absence of serum albumin. At intermediate pH values, both forms are present. Addn. of 0.2M NaCl shifts the equil. towards the high-Km form. Both forms of these enzymes are active on 4-methylumbelliferyl-.beta.-D-glucuronide and on the hexasaccharides of chondroitin 6-sulfate, chondroitin, and hyaluronic acid, with the low-Km forms showing 2- to 20-fold more activity on the oligosaccharide substrates than the high-Km forms.

IT **57323-42-9 73603-40-4**
RL: RCT (Reactant)
(reaction of, with .beta.-glucuronidase multiple forms, kinetics of)

L8 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:17858 HCAPLUS
DOCUMENT NUMBER: 92:17858
TITLE: Degradation of even-numbered reduced and non-reduced hyaluronate oligosaccharides with D-glucuronic acid or N-acetyl-D-glucosamine as non-reducing terminal by chondroitin ABC and AC lyases
AUTHOR(S): Ulrich, Hans Peter; Klein, Udo; Von Figura, Kurt
CORPORATE SOURCE: Physiol.-Chem. Inst., Univ. Muenster, Muenster, D-4400, Fed. Rep. Ger.
SOURCE: Hoppe-Seyler's Z. Physiol. Chem. (1979), 360(10), 1457-63
CODEN: HSZPAZ; ISSN: 0018-4888
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chondroitin ABC and AC lyases split hexosaminidic linkages in galactosaminoglycans and hyaluronic acid. Even-numbered oligosaccharides from hyaluronic acid with either D-glucuronic acid or N-acetylglucosamine in nonreducing position were used, prior to and after redn. with NaBH4, as substrates for chondroitin ABC and AC lyases. These substrates allowed elucidation of the effects of the nearest neighborhood of the bond to be split on the action of the enzymes. The results indicate that chondroitin ABC lyase acts strictly as an endolyase towards hyaluronate and requires the presence of a disaccharide in both reducing and non-reducing positions of the endohexosaminidic bond to be split. None of the hexosaminidic bonds of the tetrasaccharide GlcNAc-GlcA-GlcNAc-GlcA is split by chondroitin ABC lyase. In contrast, chondroitin AC lyase acts also as an exoglycosidase towards hyaluronate and recognizes only the amino sugar and the uronic acid residue that are linked via the hexosaminidic bond which is split. Thus, the N-acetylglucosamine and glucuronic acid residues at both ends of a tetrasaccharide with the structure GlcNAc-GlcA-GlcNAc-GlcA are liberated.
IT **57282-64-1**
RL: RCT (Reactant)
(reaction of, with chondroitin lyases)

L8 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1979:485843 HCAPLUS
DOCUMENT NUMBER: 91:85843
TITLE: Interactions of cartilage proteoglycans with hyaluronate. Inhibition of the interaction by modified oligomers of hyaluronate
AUTHOR(S): Christner, James E.; Brown, Martin L.; Dziewiatkowski, Dominic D.
CORPORATE SOURCE: Dent. Res. Inst., Univ. Michigan, Ann Arbor, MI, 48109, USA
SOURCE: J. Biol. Chem. (1979), 254(11), 4624-30
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Oligomers of hyaluronic acid (I) were prepd. by digestion of I from rooster combs with testicular hyaluronoglucosaminidase, leech head hyaluronoglucuronidase, and with hyaluronate lyase from Streptomyces hyalurolyticus). The oligomers were fractionated by gel permeation,

using Sephadex G-50. Oligomers isolated after incubation of I with the testicular enzyme were modified further. To prep. oligomers with N-acetylglucosamine at both ends, terminal nonreducing glucuronic acid residues were removed with .beta.-glucuronidase. Reducing terminal N-acetylglucosamine residues were removed by reaction under mildly alk. conditions. The reducing terminal N-acetylglucosamine residues also were reduced with NaBH4 to form N-acetylglucosaminitol. The potentials of the various oligosaccharides to bind to the proteoglycan from bovine nasal septum cartilage were estd. by detg. their effectiveness as inhibitors of the proteoglycan-hyaluronate interaction. In order to bind maximally to the proteoglycan, the hyaluronate oligosaccharide must be .gtoreq.10 sugar residues in length and be terminated at the nonreducing and reducing ends with a glucuronate residue and an N-acetylglucosamine residue, resp. Sugar residues extended beyond this basic decasaccharide do not interact with the hyaluronate binding site on the proteoglycan.

IT **57282-62-9 57323-43-0 71058-09-8**
71058-10-1 71058-11-2 71058-12-3
71058-13-4 71058-14-5 71058-15-6
71058-16-7 71060-23-6 71086-83-4
71086-84-5 71177-54-3
RL: BIOL (Biological study)
(proteoglycans interaction with hyaluronate inhibition by)

L8 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1975:574710 HCAPLUS
DOCUMENT NUMBER: 83:174710
TITLE: Mechanism of action of bovine testicular hyaluronidase. Mapping of the active site
AUTHOR(S): Highsmith, Stefan; Garvin, James H, Jr.; Chipman, David M.
CORPORATE SOURCE: Dep. Biol., Ben-Gurion Univ. Negev, Beer Sheva, Israel
SOURCE: J. Biol. Chem. (1975), 250(18), 7473-80
CODEN: JBCHA3
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The reactions of purified, homogeneous bovine testicular hyaluronidase were studied with radioactively labeled oligomers of hyalobiuronic acid as substrates and acceptors. Transglycosylation occurred by transfer of a glycosyl residue with retention of configuration from a leaving group to an acceptor. On the basis of detailed examn. of cleavage and transglycosylation patterns for the trimer; comparison of trimer, tetramer, and polymer as substrates; comparison of acceptors; equil. binding; and other data, it is proposed that the enzyme's active site consists of 5 subsites for hyalobiuronate residues. In the terminology of I. Schechter and A. Berger (1966), these are s2-s1-s'1-s'2-s3, where the reducing terminus is to the right, and cleavage occurs between s1 and s'1. It is proposed that subsite s'2 has a high affinity for a substrate residue, whereas s1 and s'1 have low substrate affinity, and s2 and s'3 are intermediate in affinity. This proposal has mechanistic implications. The reactions of several substrates showed similar bell-shaped pH dependences, with optima in the region of pH 5-5.5.

IT **57282-62-9 57282-64-1 57282-65-2**
57282-67-4 57323-42-9 57323-43-0
RL: BIOL (Biological study)

(hyaluronidase reaction with, active site and mechanism in relation to)

L8 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1974:516573 HCAPLUS
DOCUMENT NUMBER: 81:116573
TITLE: Preparation of tritium-labeled hyaluronic acid oligomers and their use in enzyme studies
AUTHOR(S): Highsmith, Stefan; Chipman, David M.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, Mass., USA
SOURCE: Anal. Biochem. (1974), 61(2), 557-66
CODEN: ANBCA2
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tritium-labeled oligosaccharides can be prepd. from hyaluronic acid by the Wilzbach technique with greater ease than usual by use of the specificity of hyaluronidase in the course of purifn. Labeled oligomers of hyalobiuronic acid were isolated and shown to be radiochem. homogeneous, and are used in studies of complex enzymic kinetics. The techniques used may have general use in prepg. generally labeled oligosaccharides.
IT **53272-85-8P 53272-86-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

FILE 'REGISTRY' ENTERED AT 11:55:21 ON 27 JUN 2002
L9 66 SEA FILE=REGISTRY ABB=ON PLU=ON (57323-42-9/BI OR 57323-43-0/BI OR 85425-43-0/BI OR 57282-62-9/BI OR 57282-67-4/BI OR 73603-40-4/BI OR 87142-75-4/BI OR 216065-16-6/BI OR 71177-54-3/BI OR 101205-01-0/BI OR 153984-85-1/BI OR 198191-91-2/BI OR 198191-93-4/BI OR 198191-95-6/BI OR 199943-20-9/BI OR 199943-21-0/BI OR 220222-62-8/BI OR 57282-64-1/BI OR 71058-09-8/BI OR 71058-12-3/BI OR 71058-13-4/BI OR 71058-16-7/BI OR 71060-23-6/BI OR 71086-83-4/BI OR 87147-49-7/BI OR 101312-53-2/BI OR 101312-54-3/BI OR 198191-92-3/BI OR 198191-94-5/BI OR 198191-96-7/BI OR 198191-97-8/BI OR 198191-98-9/BI OR 198191-99-0/BI OR 198192-00-6/BI OR 199943-22-1/BI OR 199943-23-2/BI OR 199943-24-3/BI OR 200053-51-6/BI OR 213611-50-8/BI OR 213899-51-5/BI OR 213899-52-6/BI OR 213899-53-7/BI OR 237058-87-6/BI OR 237058-88-7/BI OR 285560-07-8/BI OR 285560-09-0/BI OR 285560-10-3/BI OR 285560-11-4/BI OR 286427-30-3/BI OR 286427-32-5/BI OR 286427-33-6/BI OR 286427-34-7/BI OR 352210-48-1/BI OR 352210-49-2/BI OR 53272-85-8/BI OR 53272-86-9/BI OR 57282-65-2/BI OR 71058-10-1/BI OR 71058-11-2/BI OR 71058-14-5/BI OR 71058-15-6/BI OR 71086-84-5/BI OR 92758-48-0/BI OR 92758-49-1/BI OR 92758-52-6/BI OR 92758-53-7/BI OR 93957-10-9/BI OR 93957-11-0/BI OR 96359-36-3/BI)

Random RNs/Strs displayed ↓

=> d 1,3,7,11,13-15,18-20,25,26,35,36,38-40,42,44-49,51,52,59,61,65 ide

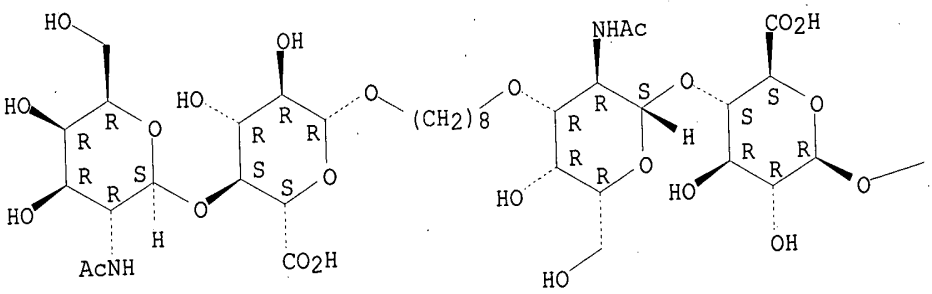
L9 ANSWER 1 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **352210-49-2** REGISTRY
CN .beta.-D-Glucopyranosiduronic acid, 4-methoxyphenyl O-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-

.beta.-D-glucopyranuronosyloxy-1,8-octanediyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyloxy-1,8-octanediyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)

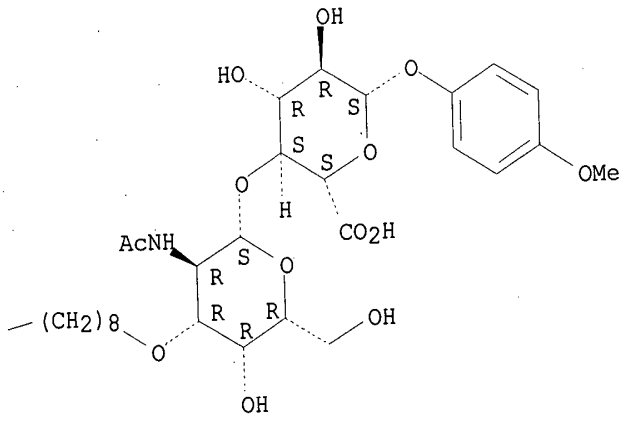
FS STEREOSEARCH
MF C65 H103 N3 O37
CI COM
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

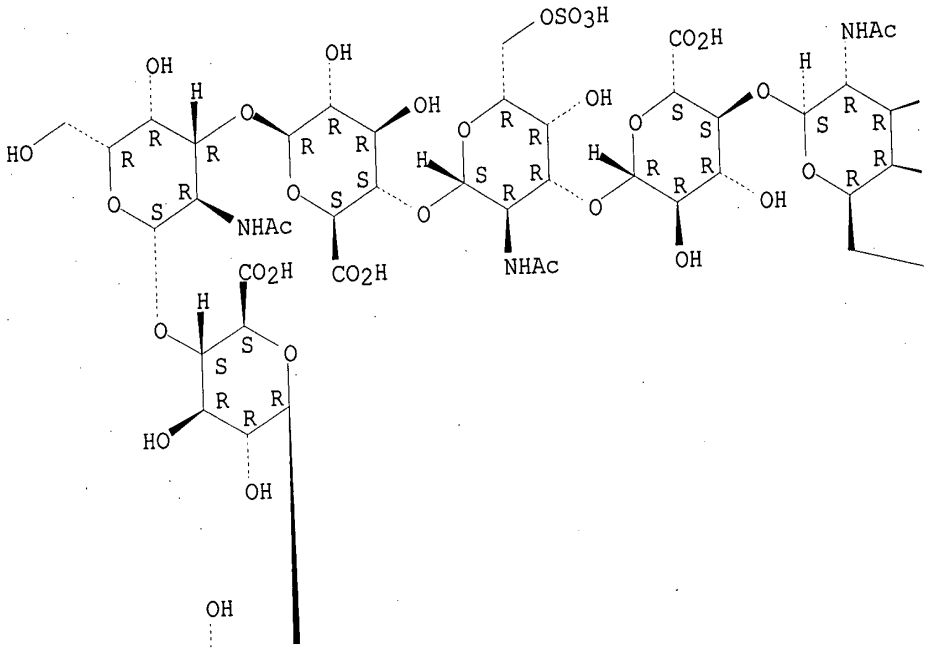
Searcher : Shears 308-4994

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

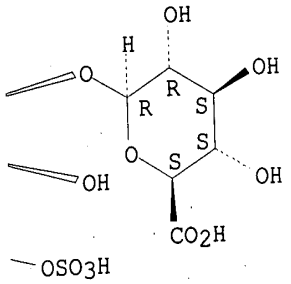
L9 ANSWER 3 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **286427-34-7** REGISTRY
CN D-Galactose, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-6-O-sulfo-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-6-O-sulfo-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C70 H107 N5 O62 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

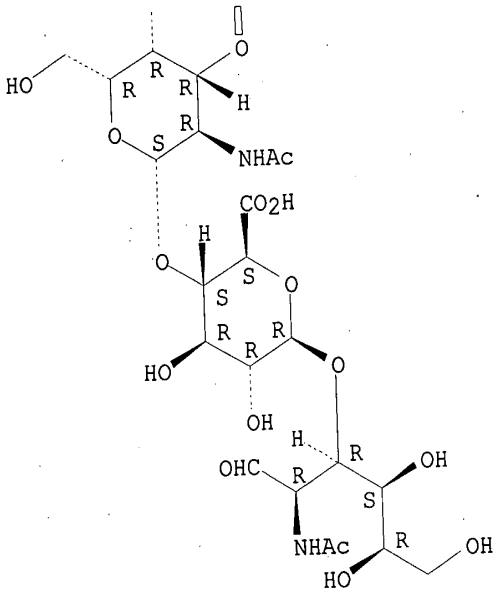
PAGE 1-A



PAGE 1-B



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

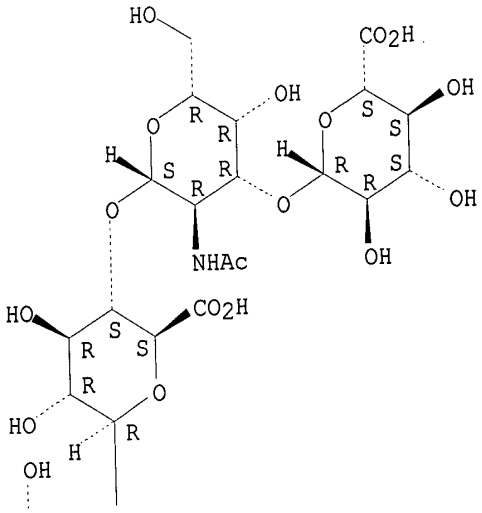
L9 ANSWER 7 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **285560-11-4** REGISTRY
CN D-Galactitol, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-1,2-dideoxy-1-(2-pyridinylamino)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH

Searcher : Shears 308-4994

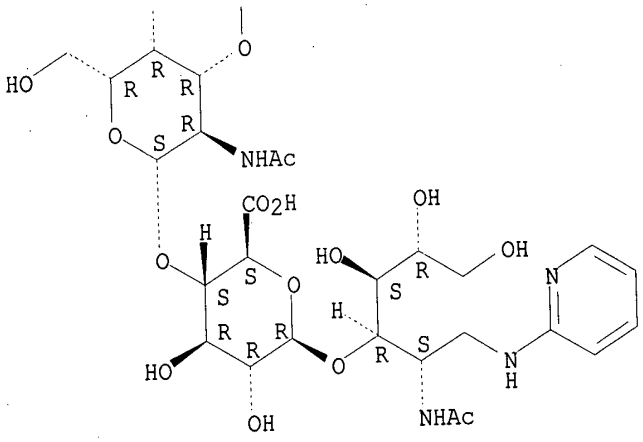
MF C47 H71 N5 O33
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



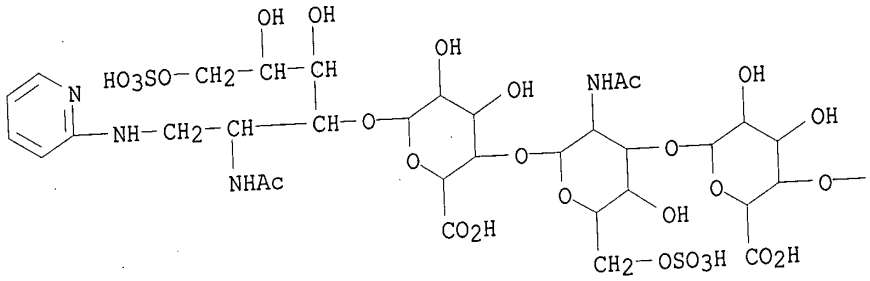
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

Searcher : Shears 308-4994

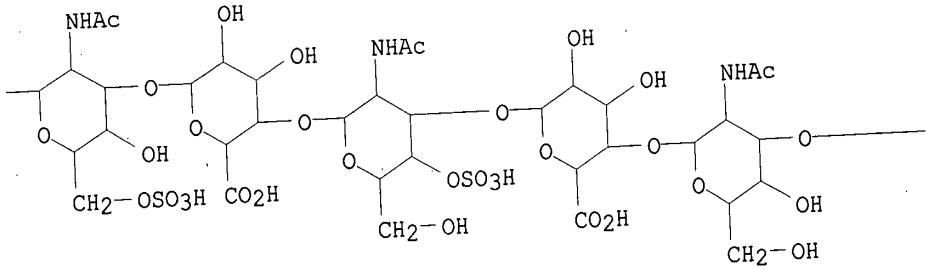
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

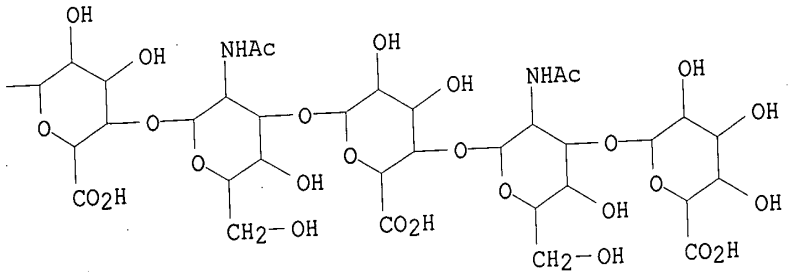
L9 ANSWER 11 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **237058-88-7** REGISTRY
CN D-Galactitol, [O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)]3-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-4-O-sulfo-.beta.-D-galactopyranosyl-(1.fwdarw.4)-[O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-6-O-sulfo-.beta.-D-galactopyranosyl-(1.fwdarw.4)]2-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-1,2-dideoxy-1-(2-pyridinylamino)-, 6-(hydrogen sulfate) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C103 H155 N9 O89 S4
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 1-B



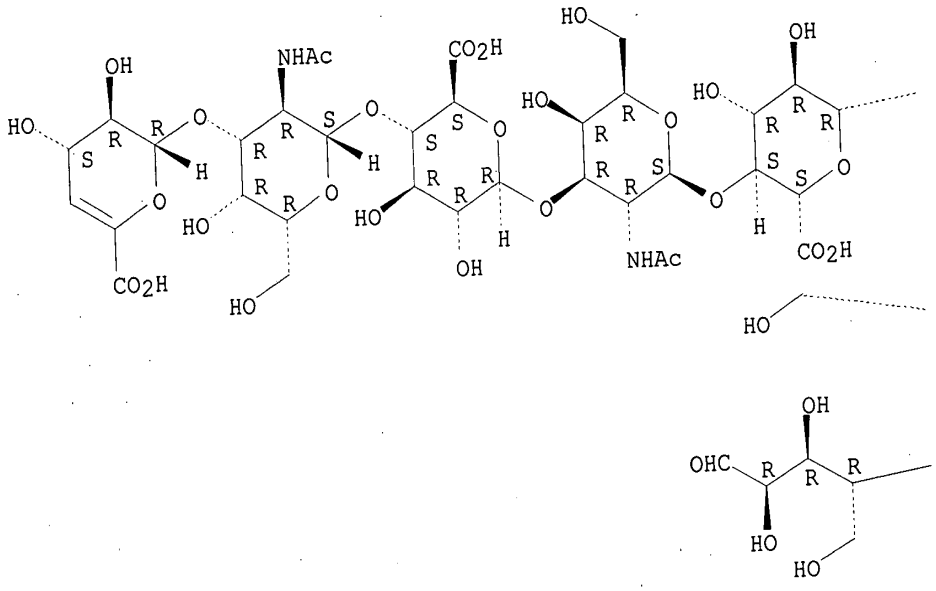


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

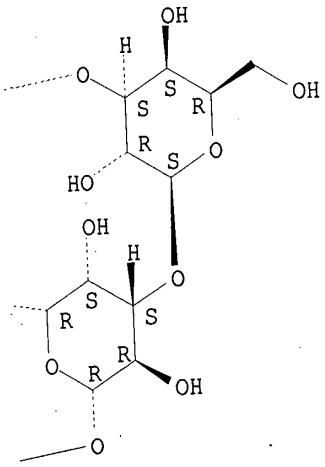
L9 ANSWER 13 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **220222-62-8** REGISTRY
CN D-Xylose, O-4-deoxy-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
DR 282523-20-0
MF C51 H78 N2 O42
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



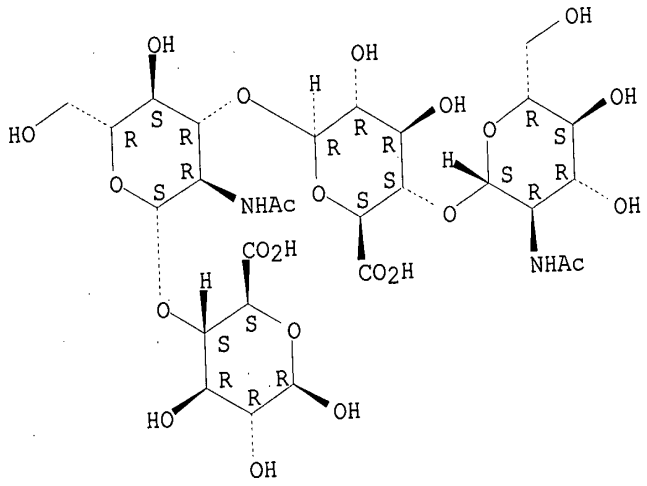
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 14 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **216065-16-6** REGISTRY

CN .beta.-D-Glucopyranuronic acid, O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H44 N2 O23
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



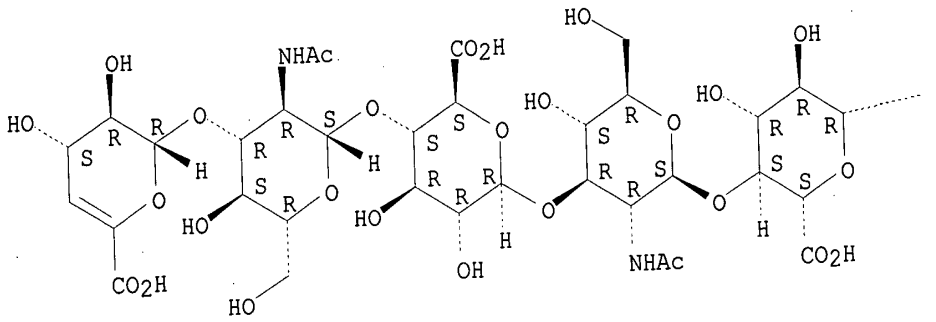
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

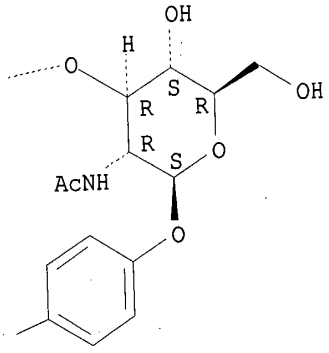
L9 ANSWER 15 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **213899-53-7** REGISTRY
CN .beta.-D-Glucopyranoside, 4-methoxyphenyl O-4-deoxy-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C49 H69 N3 O34
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

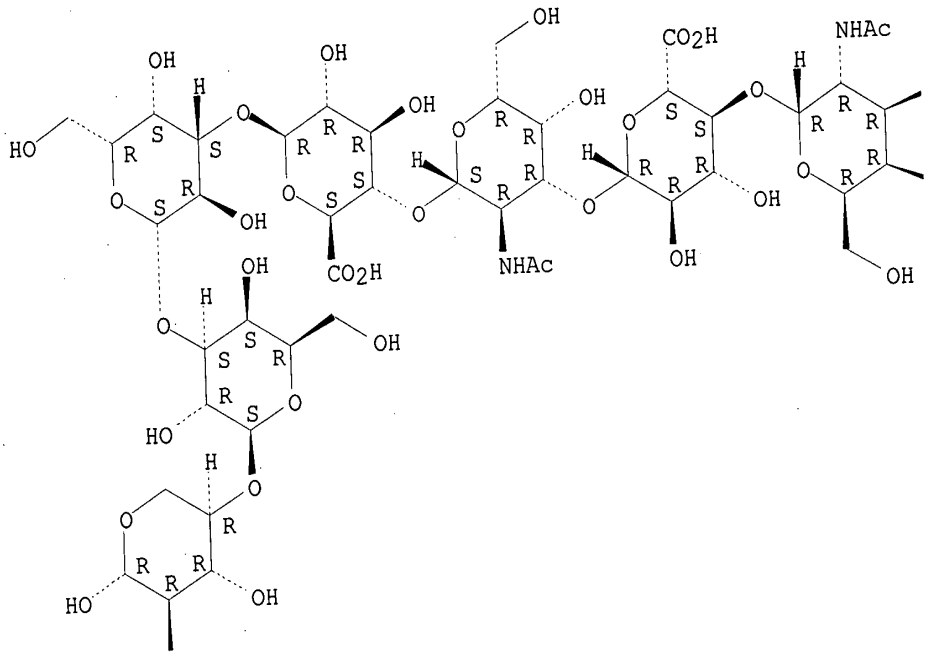
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 18 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **213611-50-8** REGISTRY
CN .beta.-D-Xylopyranose, O-2-(acetylamino)-2-deoxy-.alpha.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.3)-O-.beta.-D-galactopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C45 H72 N2 O37
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Searcher : Shears 308-4994

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

PAGE 2-A

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

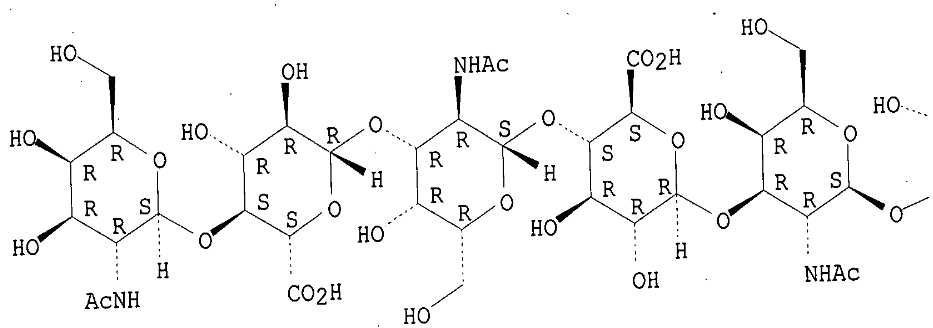
L9 ANSWER 19 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **200053-51-6** REGISTRY
CN D-Galactose, O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-

(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-
(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-
.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-
.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-
(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-
(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-
(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-
.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy-
(9CI) (CA INDEX NAME)

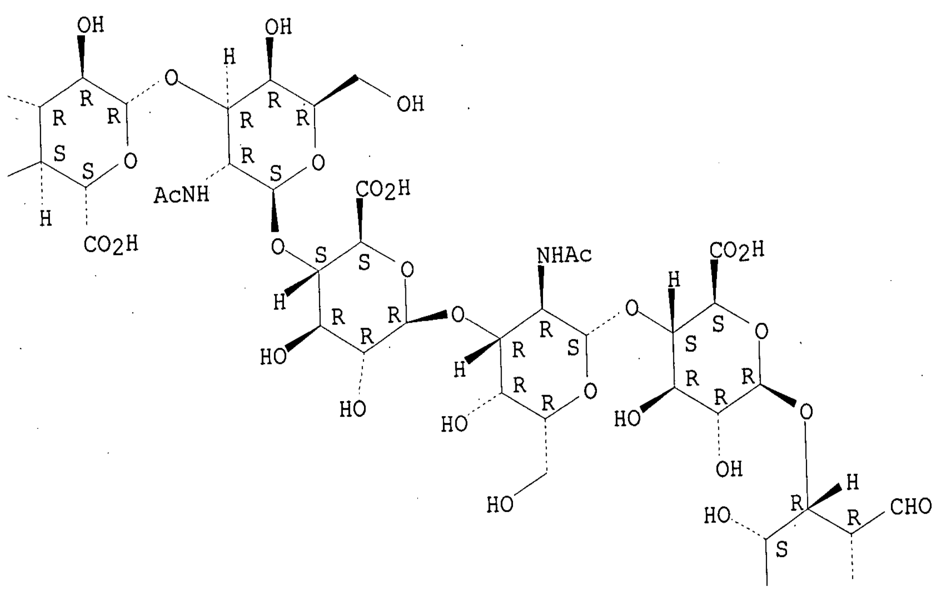
FS STEREOSEARCH
MF C78 H120 N6 O61
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

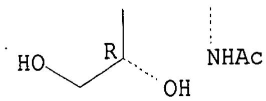
PAGE 1-A



PAGE 1-B



PAGE 2-B

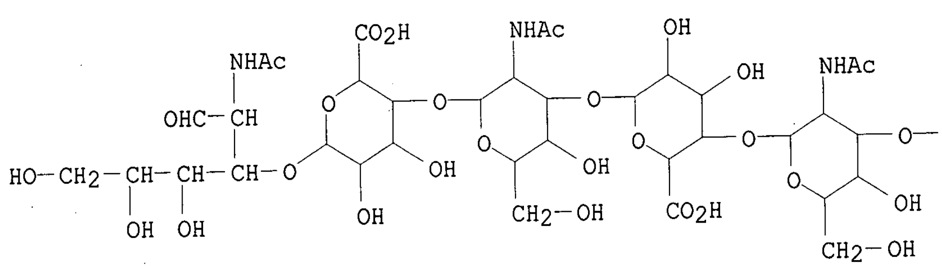


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

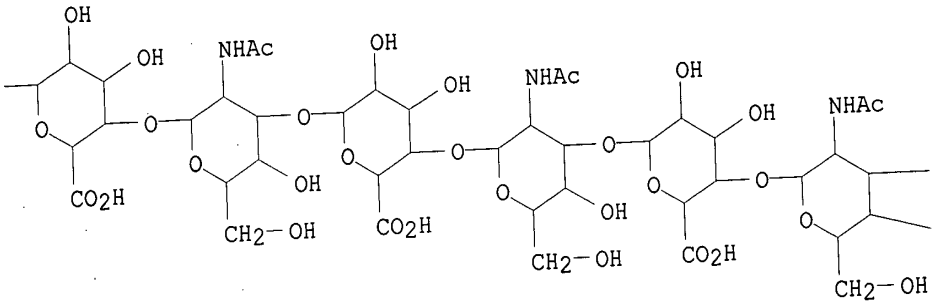
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 20 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **199943-24-3** REGISTRY
CN D-Galactose, O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C92 H141 N7 O72
SR CA
LC STN Files: CA, CAPLUS

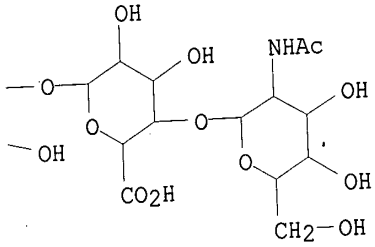
PAGE 1-A



PAGE 1-B



PAGE 1-C



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

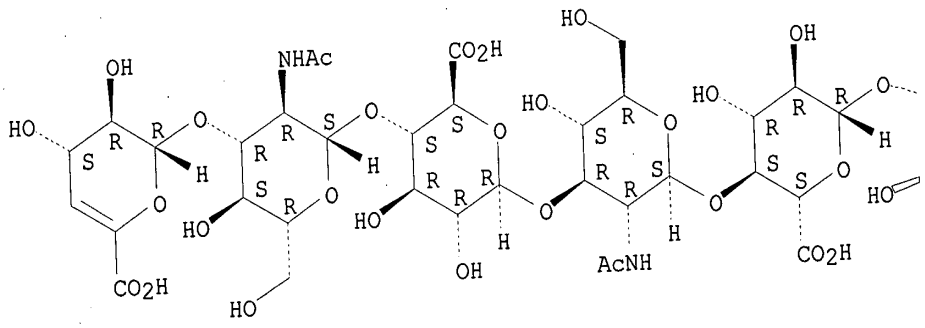
L9 ANSWER 25 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **198192-00-6** REGISTRY
CN D-Glucose, O-4-deoxy-.alpha.-L-threo-hex-4-enopyranuronosyl-
(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-
(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-
(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-
D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-
glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-
(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-
(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-
(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-
D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-
glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-
(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-
(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-

(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)

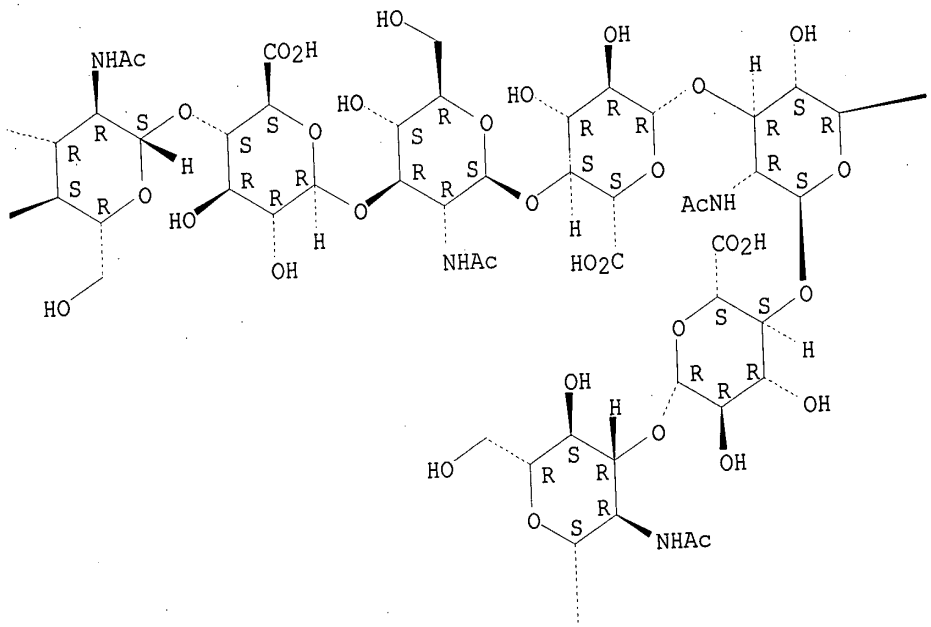
FS STEREOSEARCH
MF C112 H168 N8 O88
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

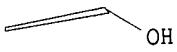
PAGE 1-A



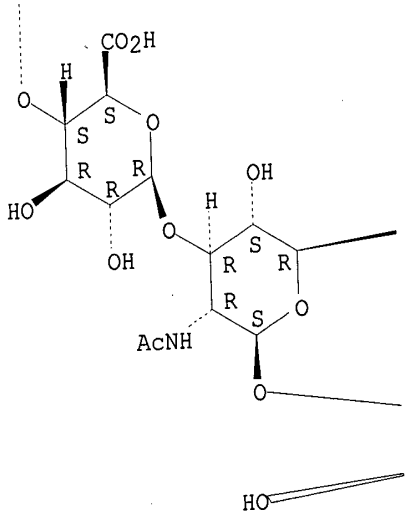
PAGE 1-B



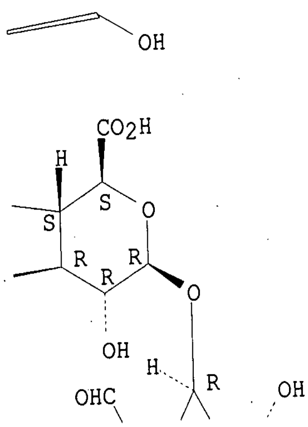
PAGE 1-C



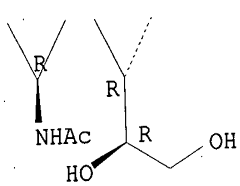
PAGE 2-B



PAGE 2-C



PAGE 3-C



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

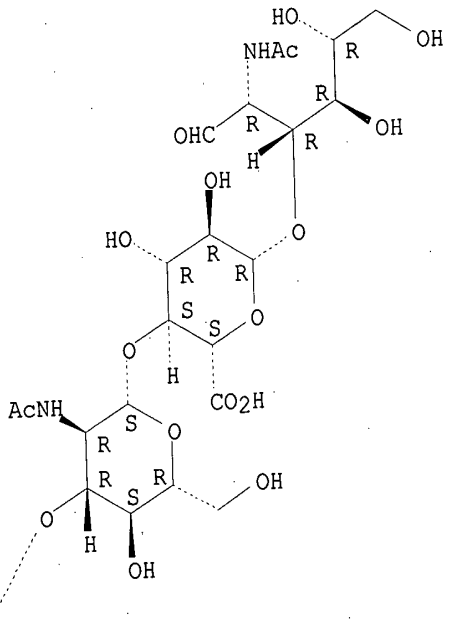
L9 ANSWER 26 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **198191-99-0** REGISTRY
CN D-Glucose, O-4-deoxy-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-

(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)

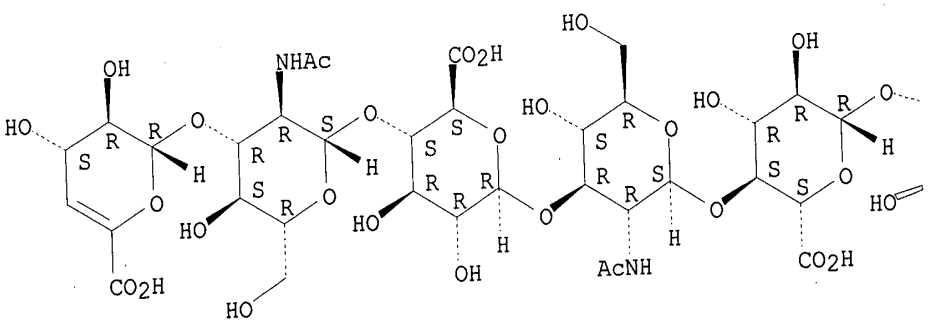
FS STEREOSEARCH
MF C98 H147 N7 O77
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

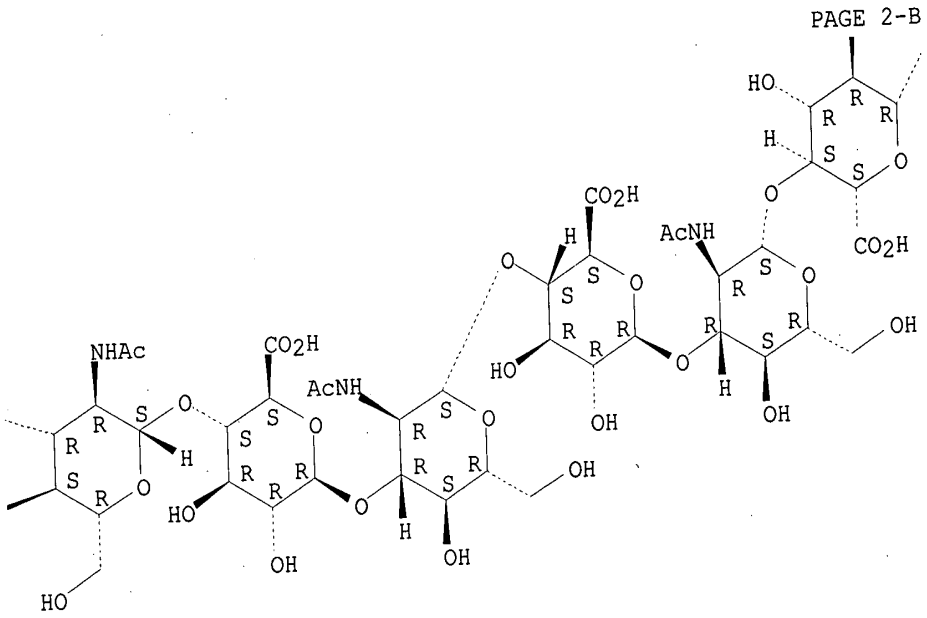
PAGE 1-C



PAGE 2-A



PAGE 2-B



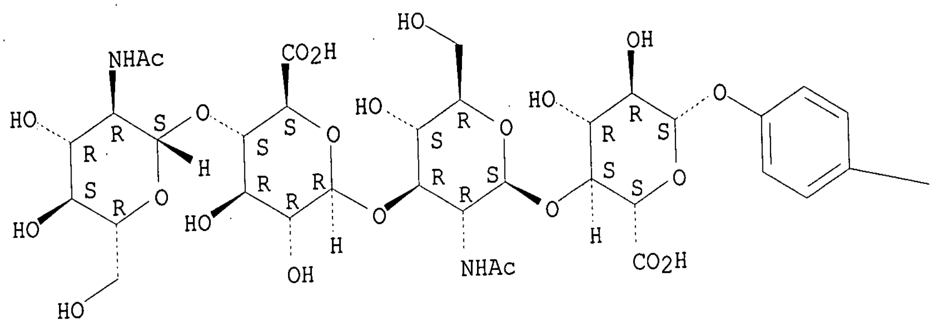
PAGE 2-C

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

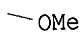
L9 ANSWER 35 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **153984-85-1** REGISTRY
CN .beta.-D-Glucopyranosiduronic acid, 4-methoxyphenyl
O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-
.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-
.beta.-D-glucopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H50 N2 O24
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

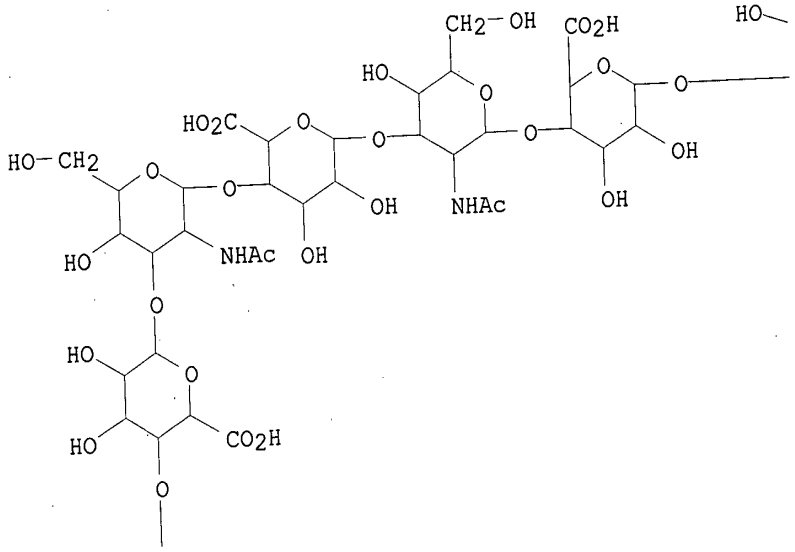


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

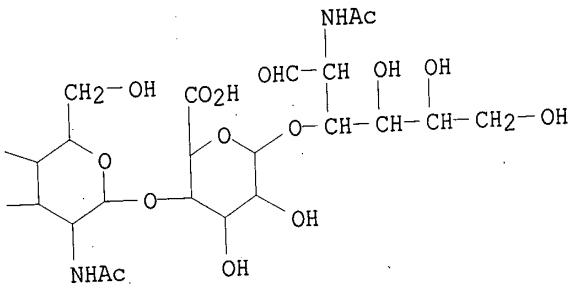
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 36 OF 66 REGISTRY
RN **101312-54-3** REGISTRY
CN D-Galactose, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
MF C70 H107 N5 O56
SR CA
LC STN Files: CA, CAPLUS

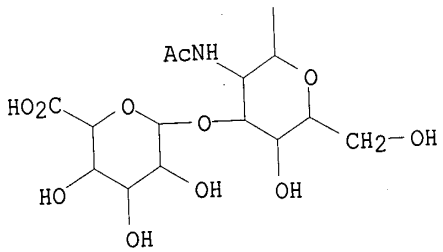
PAGE 1-A



PAGE 1-B



PAGE 2-A



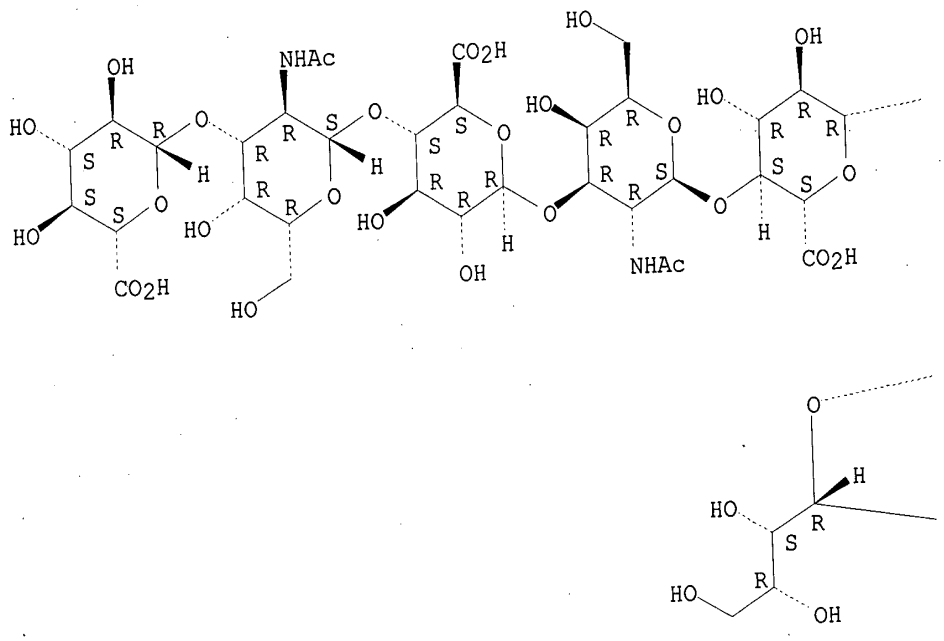
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

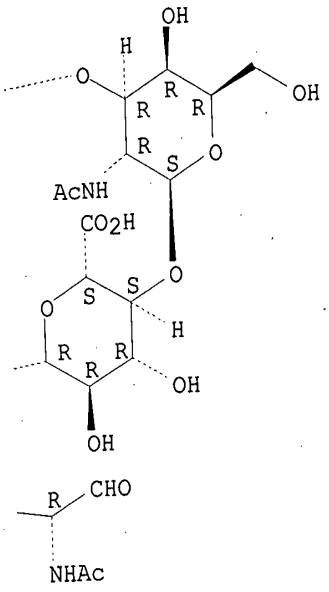
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 38 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **101205-01-0** REGISTRY
CN D-Galactose, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C56 H86 N4 O45
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A





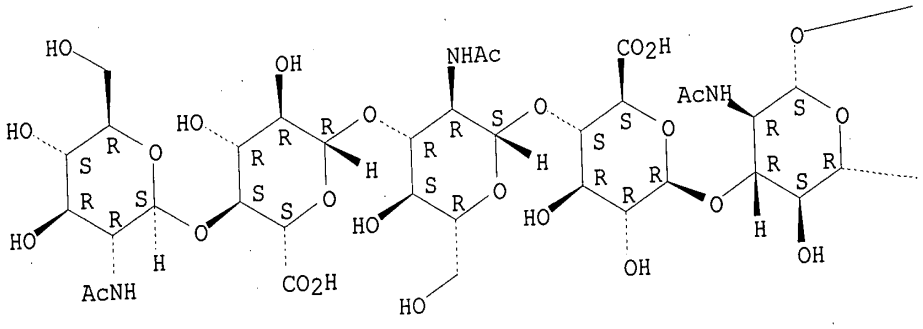
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

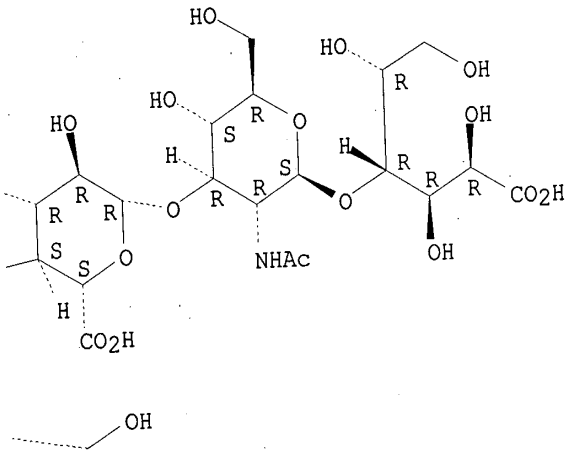
L9 ANSWER 39 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **96359-36-3** REGISTRY
CN D-Gluconic acid, O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C56 H88 N4 O45
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

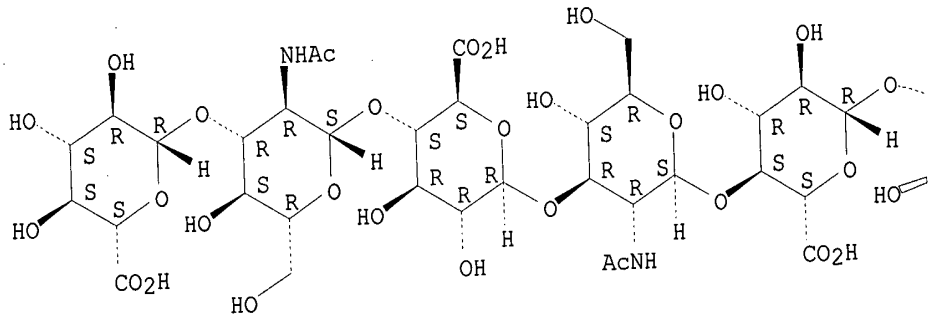
L9 ANSWER 40 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **93957-11-0** REGISTRY
CN D-Glucose, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-

glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-
(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-
(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-
(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-
D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-
glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-
(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-
(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-
(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-
D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI)
(CA INDEX NAME)

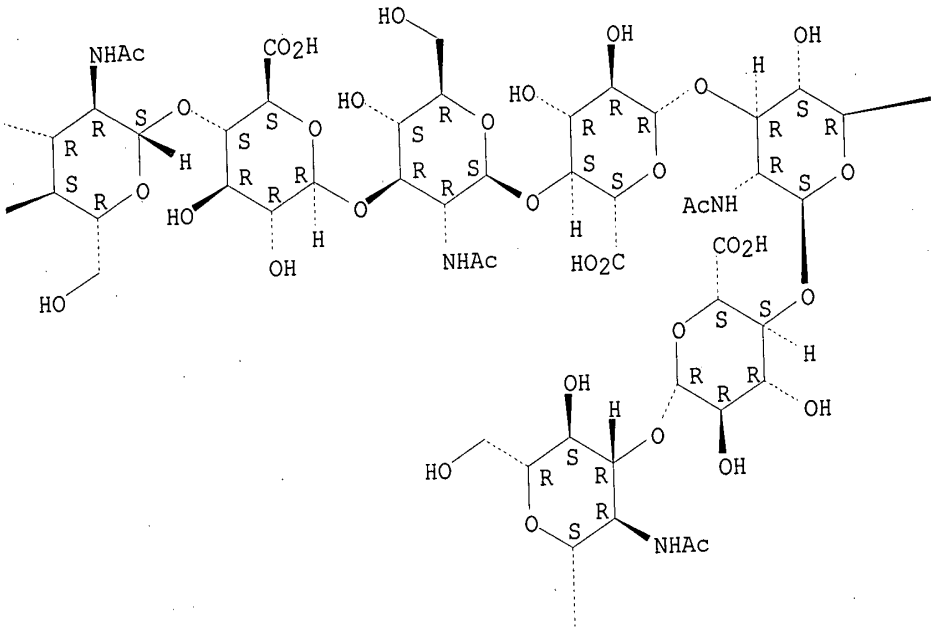
FS STEREOSEARCH
MF C112 H170 N8 O89
CI COM
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

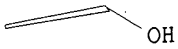
PAGE 1-A



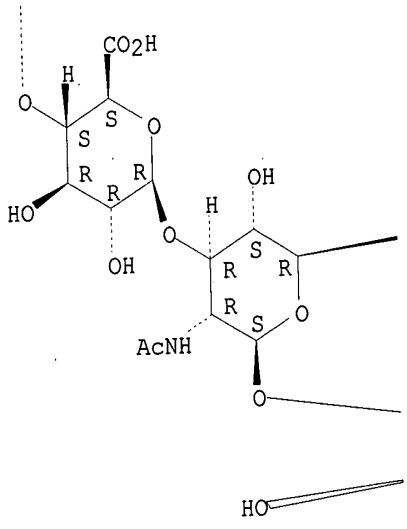
PAGE 1-B



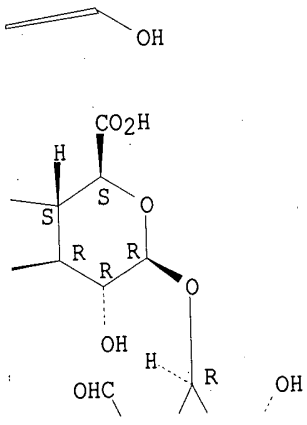
PAGE 1-C



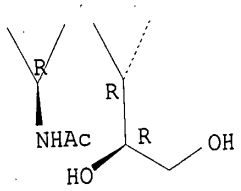
PAGE 2-B



PAGE 2-C



PAGE 3-C



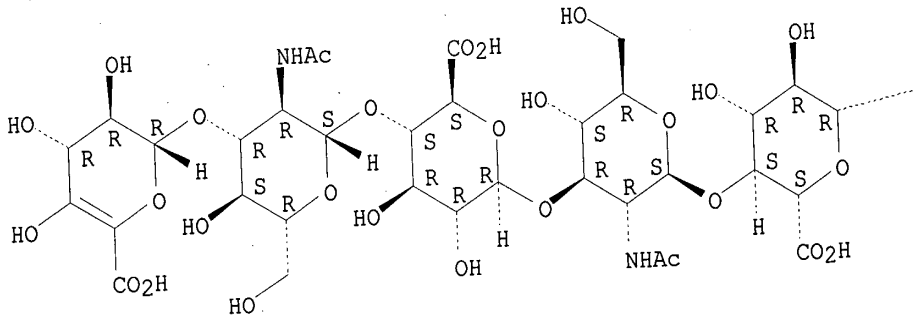
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

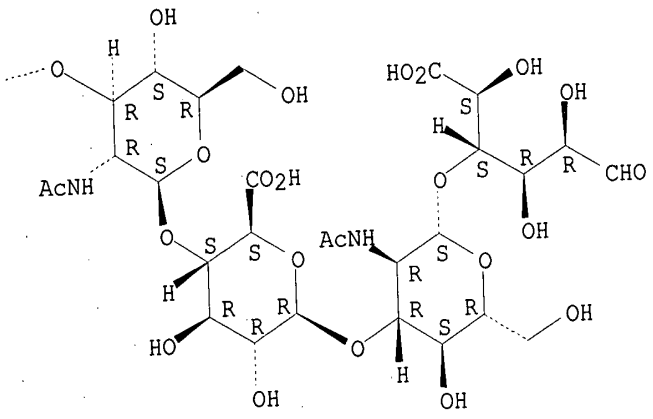
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 42 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **92758-53-7** REGISTRY
CN D-Glucuronic acid, O-.alpha.-L-threo-hex-4-enopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C62 H92 N4 O51
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A





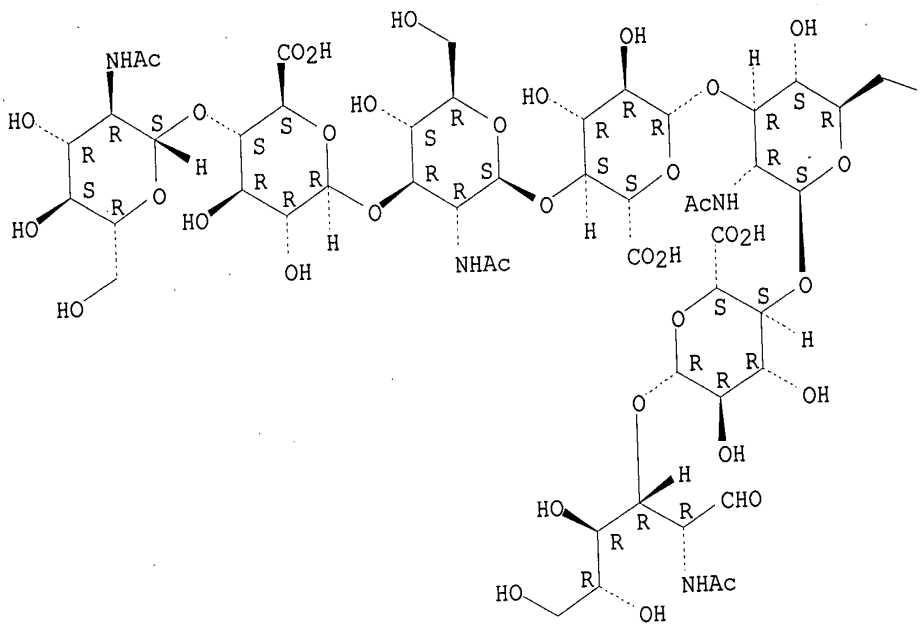
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 44 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **87147-49-7** REGISTRY
CN D-Glucose, O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C50 H78 N4 O39
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

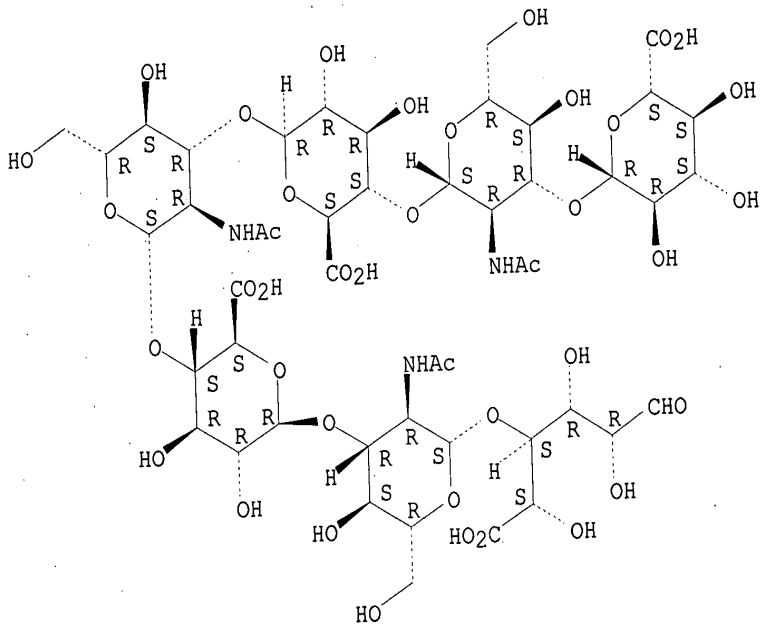
OH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 45 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **87142-75-4** REGISTRY
CN D-Glucuronic acid, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C48 H73 N3 O40
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



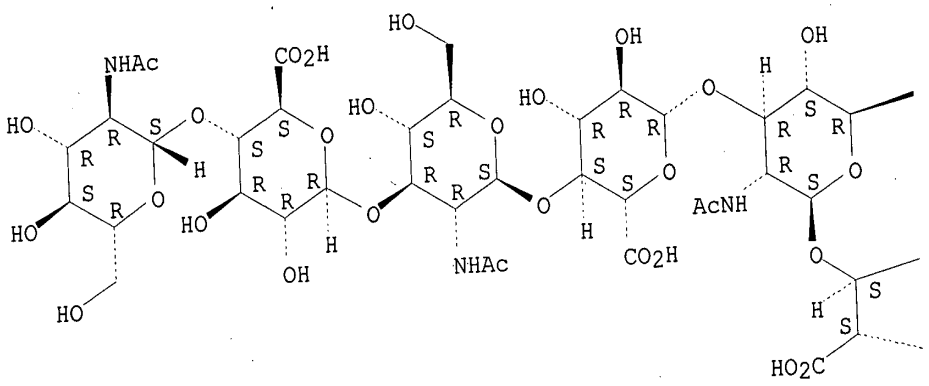
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

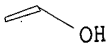
L9 ANSWER 46 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **85425-43-0** REGISTRY
CN D-Glucuronic acid, O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C42 H65 N3 O34
LC STN Files: CA, CAPLUS

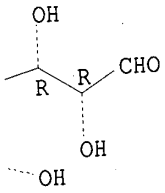
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



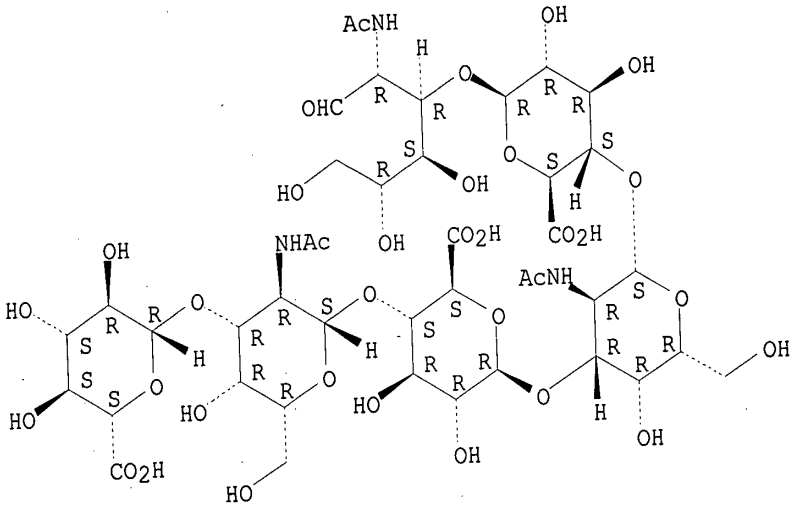


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 47 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **73603-40-4** REGISTRY
CN D-Galactose, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C42 H65 N3 O34
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



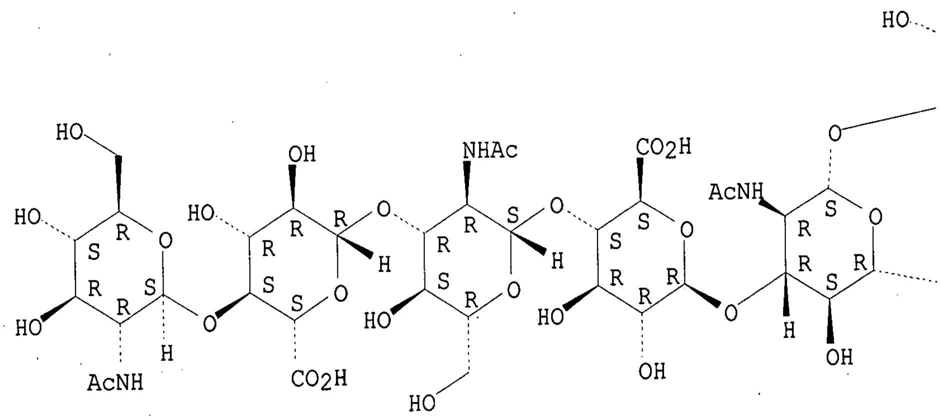
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

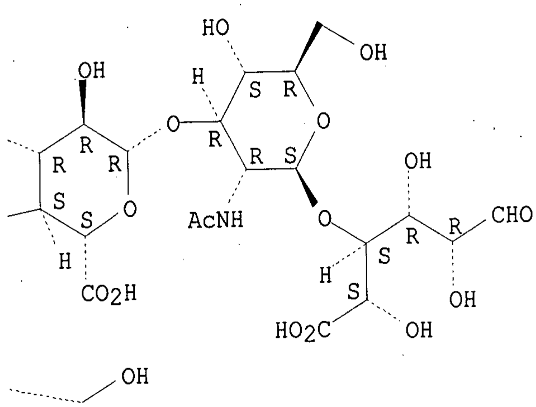
L9 ANSWER 48 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **71177-54-3** REGISTRY
CN D-Glucuronic acid, O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C56 H86 N4 O45
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

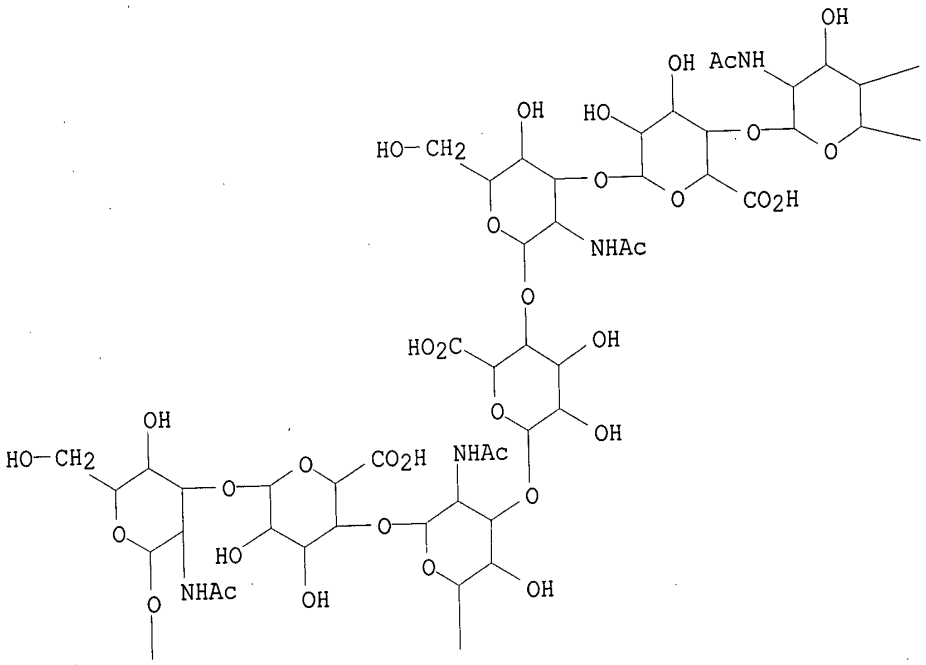
L9 ANSWER 49 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **71086-84-5** REGISTRY
CN D-Glucuronic acid, O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-

(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)

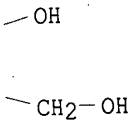
MF C84 H128 N6 O67

LC STN Files: CA, CAPLUS

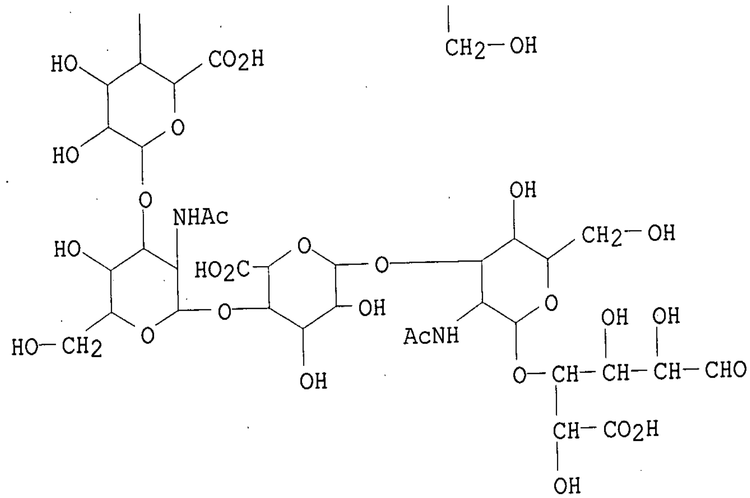
PAGE 1-A



PAGE 1-B



PAGE 2-A



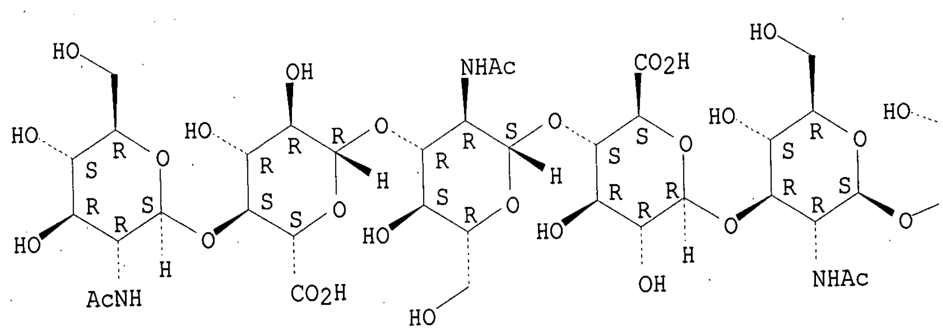
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

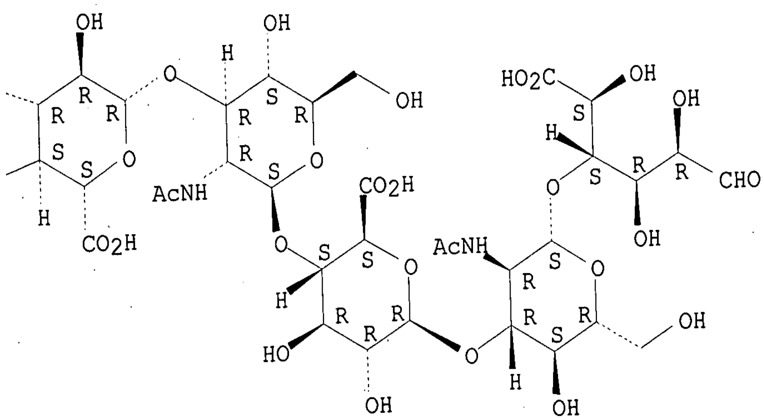
L9 ANSWER 51 OF 66 REGISTRY
RN **71060-23-6** REGISTRY
CN D-Glucuronic acid, O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C70 H107 N5 O56
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



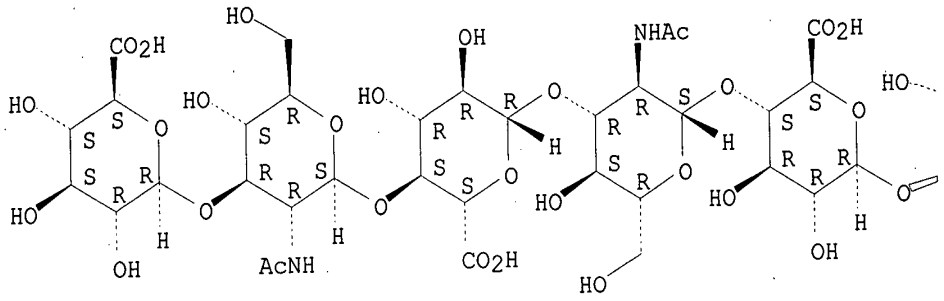
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

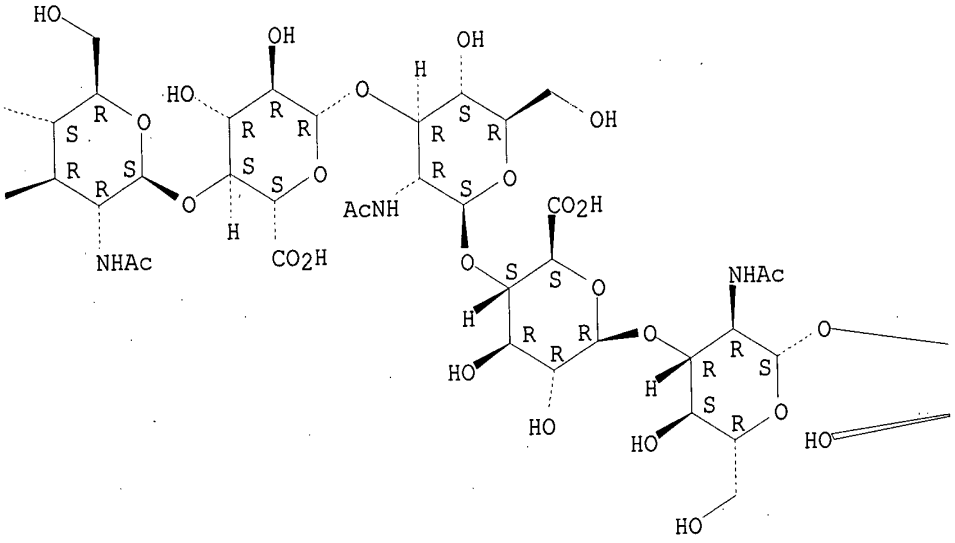
L9 ANSWER 52 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **71058-16-7** REGISTRY
CN D-Glucose, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C84 H128 N6 O67
CI COM
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

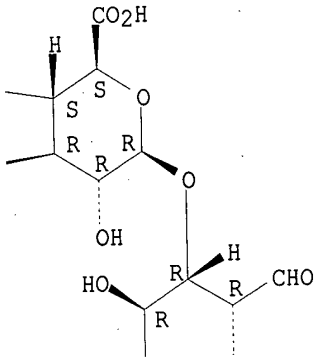
PAGE 1-A



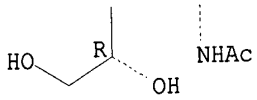
PAGE 1-B



PAGE 1-C



PAGE 2-C



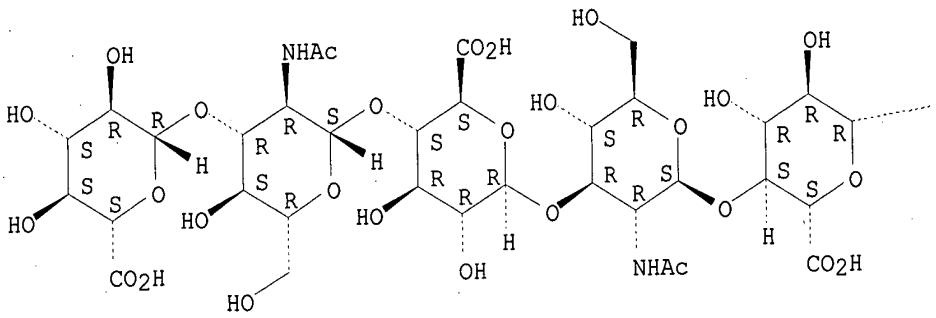
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

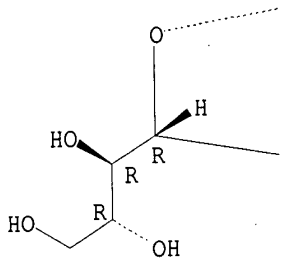
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 59 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **57323-43-0** REGISTRY
CN D-Glucose, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C56 H86 N4 O45
CI COM
LC STN Files: CA, CAPLUS

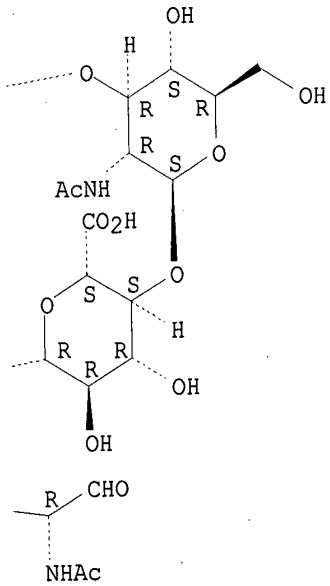
Absolute stereochemistry.

PAGE 1-A





PAGE 1-B

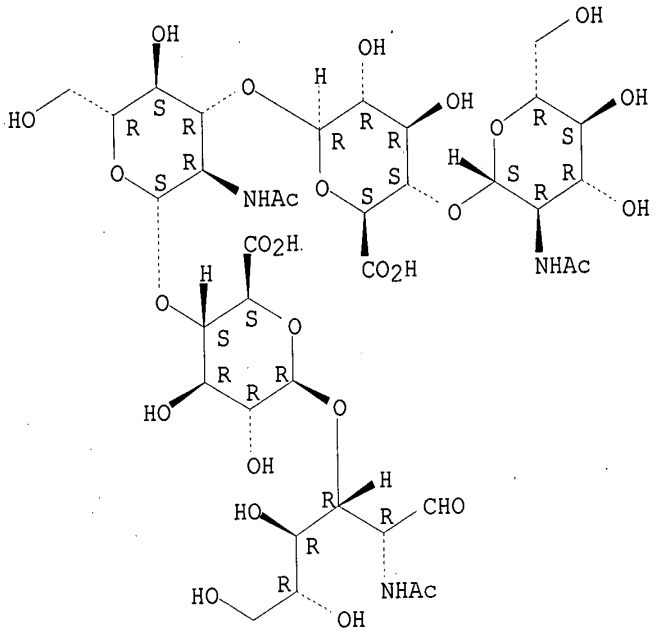


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 61 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **57282-67-4** REGISTRY
CN D-Glucose, O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H57 N3 O28
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

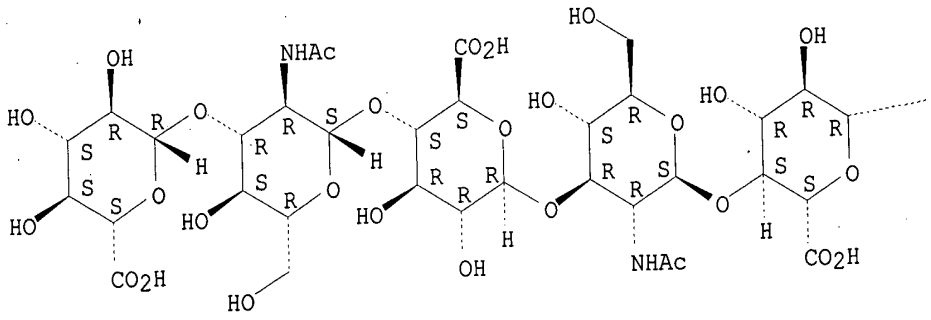
L9 ANSWER 65 OF 66 REGISTRY COPYRIGHT 2002 ACS
RN **53272-86-9** REGISTRY
CN D-Glucose, O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-

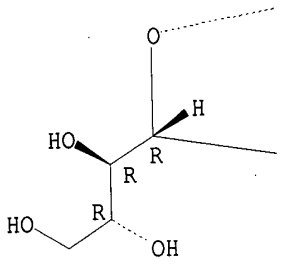
(1.fwdarw.4)-O-.beta.-D-glucopyranuronosyl-(1.fwdarw.3)-2-(acetylamino)-2-deoxy-, labeled with tritium (9CI) (CA INDEX NAME)

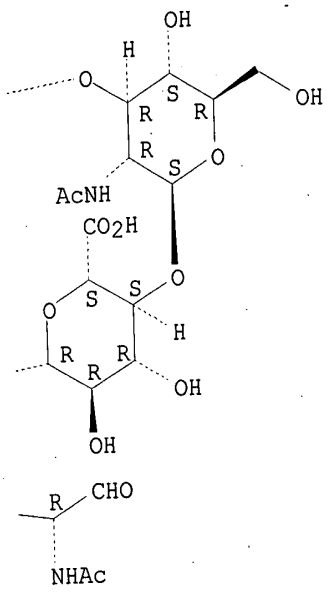
FS STEREOSEARCH
MF C56 H86 N4 O45
LC STN Files: CA, CAPLUS
IL XH-3

Absolute stereochemistry.

PAGE 1-A





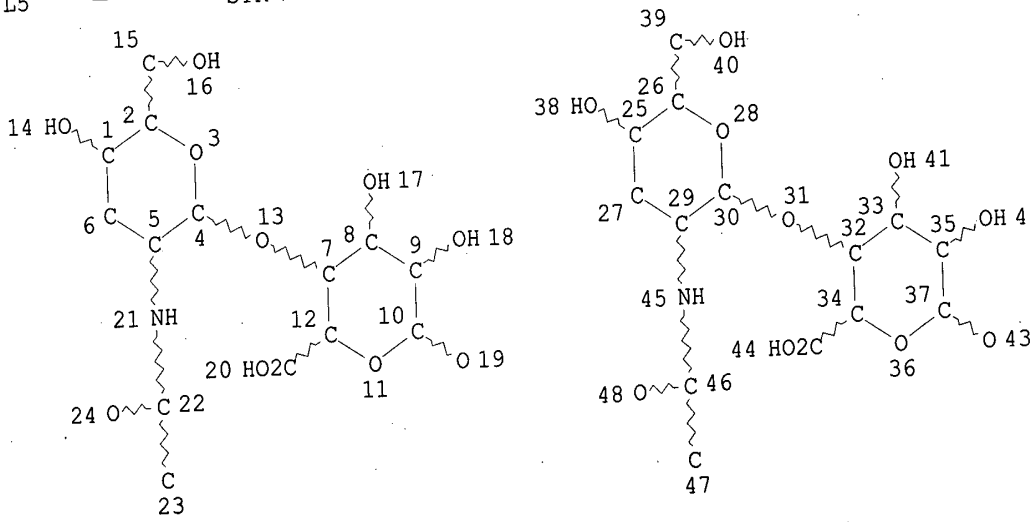


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

FILE 'CAOLD' ENTERED AT 11:57:36 ON 27 JUN 2002
L10 0 S L9

FILE 'USPATFULL' ENTERED AT 11:57:41 ON 27 JUN 2002
L11 0 S L9

(FILE 'MARPAT' ENTERED AT 11:57:59 ON 27 JUN 2002)
L5 STR



Page 1-A

2

Page 1-B
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 48

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
MLEVEL IS CLASS ON RING NODES AND RING GROUPS
MLEVEL IS CLASS ON CHAIN NODES AND CHAIN GROUPS
ECLEVEL IS UNLIM ON ALL NODES

L14 35 SEA FILE=MARPAT SSS FUL L5 (MODIFIED ATTRIBUTES)

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
MLEVEL IS CLASS ON RING NODES AND RING GROUPS
MLEVEL IS CLASS ON CHAIN NODES AND CHAIN GROUPS
ECLEVEL IS UNLIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L15 16 SEA FILE=MARPAT SUB=L14 SSS FUL L5 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 35 ITERATIONS (7 INCOMPLETE) 16 ANSWERS
SEARCH TIME: 00.00.21

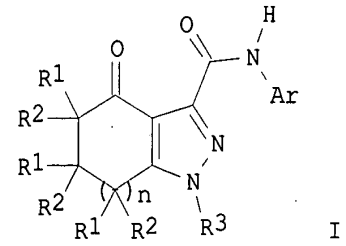
L15 ANSWER 1 OF 16 MARPAT COPYRIGHT 2002 ACS
(ALL HITs ARE ITERATION INCOMPLETES)
ACCESSION NUMBER: 136:247578 MARPAT
TITLE: Preparation of aryl substituted tetrahydroindazoles and their use as ligands for the GABAA receptor
INVENTOR(S): Maynard, George; Albaugh, Pamela; Rachwal, Stanislaw; Gustavson, Linda M.
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020492	A1	20020314	WO 2001-US27676	20010906

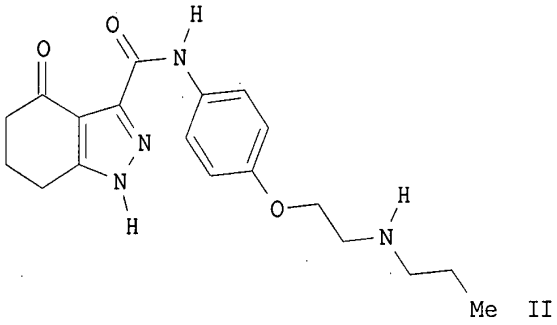
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,

KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002055524 A1 20020509 US 2001-947702 20010906
PRIORITY APPLN. INFO.: US 2000-230256P 20000906
GI



I



II

AB Title compds. I [R1 and R2 = independently H, halo, OH, alkyl, alkenyl, CN, etc.; n = 0-2; R3 = H, alkyl; Ar = (un)substituted aryl or a satd., unsatd., or arom. heterocyclic group] and the pharmaceutically acceptable salts are prepd. and disclosed as ligands for the GABAA receptor. Thus, II was prepd. via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation with [2-(4-aminophenoxy)-ethyl]propylcarbamic acid tert-Bu ester. Methods for assaying GABAA binding affinity and evaluation of agonist, antagonist or inverse agonist behavior are described (no data). A method for demonstrating the presence of GABAA receptors in cell or tissue samples is also claimed. These compds. are highly selective agonists, antagonists or inverse agonists for GABAA brain receptors or prodrugs of agonists, antagonists or inverse agonists for GABAA brain receptors and are therefore useful in the diagnosis and treatment of anxiety, depression, Down Syndrome, sleep and seizure disorders, overdose with benzodiazepine drugs and for enhancement of memory.

IC ICM C07D231-56
ICS C07D401-12; A61K031-416; A61K031-4439

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

ST indazole aryltetrahydro prepn GABA receptor ligand;

aryltetrahydroindazole prepn GABA receptor ligand; GABA receptor analysis method

IT GABA agonists
GABA antagonists
(GABAA; prepn. of GABAA receptor ligands aryl substituted tetrahydroindazoles via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation)

IT GABA receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GABAA; prepn. of GABAA receptor ligands aryl substituted tetrahydroindazoles via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation)

IT Sleep
(disorder; prepn. of GABAA receptor ligands aryl substituted tetrahydroindazoles via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation)

IT Anticonvulsants
Antidepressants
Anxiolytics
Human
(prepn. of GABAA receptor ligands aryl substituted tetrahydroindazoles via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation)

IT Alzheimer's disease
(treatment of Alzheimer's dementia; prepn. of GABAA receptor ligands aryl substituted tetrahydroindazoles via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation)

IT Down's syndrome
(treatment; prepn. of GABAA receptor ligands aryl substituted tetrahydroindazoles via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation)

IT 3383-72-0P 16365-27-8P 19499-60-6P 60814-17-7P 96546-39-3P
194098-60-7P 194098-61-8P 194098-62-9P 282541-68-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of GABAA receptor ligands aryl substituted tetrahydroindazoles via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation)

IT 100-02-7, p-Nitrophenol, reactions 100-11-8, p-Nitrobenzyl bromide
407-25-0, Trifluoroacetic anhydride 18157-17-0,
2-Chloroethoxytrimethylsilane 96546-37-1 403740-99-8
403741-00-4 403741-01-5 403741-02-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of GABAA receptor ligands aryl substituted tetrahydroindazoles via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation)

IT 403740-89-6P 403740-90-9P 403740-91-0P 403740-92-1P
403740-93-2P 403740-94-3P 403740-95-4P 403740-96-5P
403740-97-6P 403740-98-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of GABAA receptor ligands aryl substituted tetrahydroindazoles via cyclocondensation of hydrazine with ethyloxalylcyclohexan-1,3-dione with subsequent redn. and amidation)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

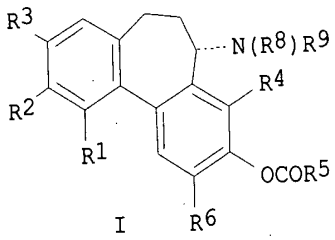
L15 ANSWER 2 OF 16 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:102557 MARPAT
TITLE: Preparation of colchinol derivatives as vascular damaging agents
INVENTOR(S): Arnould, Jean Claude; Lamorlette, Maryannick Andree
PATENT ASSIGNEE(S): Angiogene Pharmaceuticals Limited, UK
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004434	A1	20020117	WO 2001-GB2966	20010704

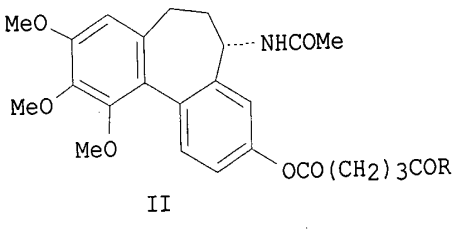
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2000-401978 20000707
GI



I



II

AB Colchinol derivs., such as I [R1 - R3 = OH, phosphoryloxy, alkoxy; R4 = R6 = H, NO2, NH2, alkylamino, OH, F, alkoxy, alkyl; R5 =

A-X-Y-B; A = alkylene, (CH2)p-Q; p = 1-2; Q = phenylene, thienylene; X = O, CO, ester, amide, amino, etc.; Y = alkylene; B = carboxy, sulfo, phosphoryloxy, hydroxy, amino, heterocyclic group, etc.; R8 = CO, ester, amino, amide, SO2, etc.; R9 = H, alkyl], and pharmaceutically acceptable salt, solvate or pro-drug thereof, were prepd. for their use as vascular damaging agents in a warm blooded animal. Thus, reaction between glutaric anhydride and N-acetylpiperazine yielded 5-(4-acetylpiperazin-1-yl)-5-oxopentanoic acid which on condensation with N-acetyl colchinol afforded colchinol deriv. II (R = 4-acetylpiperazin-1-yl). The prepd. colchinol derivs. were tested against s.c. CaNT tumors.

IC ICM C07D295-16
ICS C07D295-18; C07D295-14; C07D211-62; C07C235-74; A61K031-495; A61K031-16; A61K031-44

CC 31-2 (Alkaloids)
Section cross-reference(s): 1

ST colchinol deriv prepn vascular damaging agent antiangiogenic antitumor

IT Angiogenesis inhibitors
Antitumor agents
(colchinol derivs. as vascular damaging agents)

IT 389056-39-7P 389056-40-0P 389056-41-1P 389056-42-2P
389056-43-3P 389056-44-4P 389056-45-5P 389056-46-6P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(colchinol derivs. as vascular damaging agents)

IT 108-30-5, Succinic anhydride, reactions 108-55-4, Glutaric anhydride 619-45-4, Methyl 4-aminobenzoate 1118-02-1, Trimethylsilyl isocyanate 13889-98-0, N-Acetylpiperazine 25503-90-6 38838-26-5, N-Acetylcolchinol 55480-45-0 57260-71-6, N-tert-Butoxycarbonyl piperazine 169527-49-5 389056-56-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(colchinol derivs. as vascular damaging agents)

IT 296245-20-0P 389056-47-7P 389056-48-8P 389056-49-9P
389056-50-2P 389056-51-3P 389056-52-4P 389056-53-5P
389056-54-6P 389056-55-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(colchinol derivs. as vascular damaging agents)

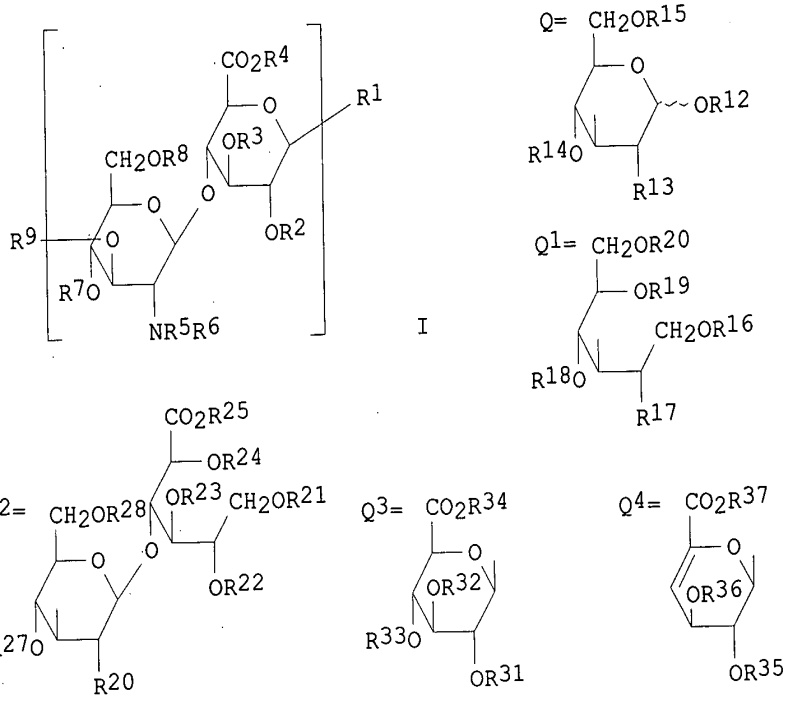
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 16 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 134:266518 MARPAT
TITLE: Preparation of oligosaccharide derivatives containing glucuronic acid and glucosamine as sebum production inhibitors
INVENTOR(S): Yatsuka, Nobuaki; Sato, Nobuyuki; Nishikawa, Masazumi; Tamai, Tadakazu; Moriyama, Shigeru
PATENT ASSIGNEE(S): Maruha Corp., Japan
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022971	A1	20010405	WO 2000-JP6638	20000927
W: AE, AL, AU, BA, BG, BR, CA, CN, CU, CZ, DZ, HR, HU, ID, IL, IN, IS, KR, LK, MA, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, US, VN, YU, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 2001097867	A2	20010410	JP 1999-272022	19990927
PRIORITY APPLN. INFO.:			JP 1999-272022	19990927

GI



AB Sebum prodn. inhibitors, which contain as the active ingredient compds. having glucuronic acid derivs. and glucosamine derivs. in the structure as represented by general formula [I; R1 = protecting group, OR10, NHR11, CH2R11, SR11 (wherein R10 = H, protecting group, Q, Q1, Q2; R11 = H, protecting group; provided that when R10 and R11 are H or protecting group, R1 and CO2R4 are in cis or trans-disposition or when R10 is Q-Q2, R12-R28 excluding R13, R17, and R26 are H or protecting group and R13, R17, and R26 are N3 or optionally protected NH2); R2-R8 = H, protecting group; R9 = H, protecting group, Q3, Q4 (wherein R31-R37 = H, protecting group); n = 0-25, provided that when n = 0, then R1 = OR10, R10 = Q2, and R9 = Q3 or Q4; the protecting group in I and Q1-Q4 is (un)substituted linear or branched C1-8 or C2-8 alkyl, (un)substituted C1-8 acyl,

arom. acyl, or arom. alkyl; or any two of R2-R37 protecting groups excluding R13, R17, and R26 together form (un)substituted C3-8 alkylidene, benzylidene, or phthaloyl; when n.gtoreq.2, then R2-R8 are same or different for each repeating unit] or pharmacol. acceptable salts, are described. These compds. are useful for the prevention or treatment of diseases caused by excessive prodn. of sebum such as acne, dandruff, and hair loss and also for cosmetics solving cosmetic problems caused by excessive prodn. of sebum, e.g. aging odor. Thus, 30 g sodium hyaluronate was dissolved in 3 L distd. water, warmed to 40.degree., adjusted to pH 6.0 with 0.1 M NaOH, treated with hyaluronidase at 0.5 turbidity redn. unit/1 mg sodium hyaluronate, allowed to react at 40.degree. for 100 h, subjected to ultrafiltration for removing the enzyme, and lyophilized to give a hydrolyzate (27.4 g) which was purified by anion-exchange chromatog. using a YMC-Pack IEC-AX column to give 1.7 g .DELTA.HexA.beta.1.fwdarw.3GlcNAc.beta.1.fwdarw.4GlcA.beta.1.fwdarw.3GlcNAc.2Na [II; .DELTA.HexA = 4-deoxy-.alpha.-L-threo-hex-4-enpyranuronosyl, i.e. Q4 (wherein R35 = R36 = H)], 5.9 g .DELTA.HexA.beta.1.fwdarw.3GlcNAc.beta.1.fwdarw.4GlcA.beta.1.fwdarw.3GlcNAc.beta.1.fwdarw.4GlcA.beta.1.fwdarw.3GlcNAc.3Na (III), 3.4 g .DELTA.HexA.beta.1.fwdarw.3GlcNAc.beta.1.fwdarw.4GlcA.beta.1.fwdarw.3GlcNAc.beta.1.fwdarw.4GlcA.beta.1.fwdarw.3GlcNAc.4Na (IV), and 2.2 g .DELTA.HexA.beta.1.fwdarw.3GlcNAc.beta.1.fwdarw.4GlcA.beta.1.fwdarw.3GlcNAc.beta.1.fwdarw.4GlcA.beta.1.fwdarw.3GlcNAc.beta.1.fwdarw.4GlcA.beta.1.fwdarw.3GlcNAc.5Na (V). II, III, IV, and V in vitro inhibited the prodn. of sebum in auricular sebaceous gland-contg. tissue from hamsters by 15.7, 28.6, 48.5, and 53.4%, resp. at 0.01%.

IC ICM A61K031-7012
ICS A61K031-702; A61K031-728; A61K007-00; A61K007-06; A61P017-08; A61P017-10; C07H015-04; C07H007-033; C08B037-08

CC 33-8 (Carbohydrates)
Section cross-reference(s): 1, 62, 63

ST oligosaccharide prepn sebum prodn inhibitor 34512

IT Aging, animal
(odor assocd. with; prepn. of oligosaccharide derivs. contg. glucuronic acid and glucosamine as sebum prodn. inhibitors for prevention or treatment of diseases caused by excessive prodn. of sebum)

IT Acne
Alopecia
Dandruff
Sebum
(prepn. of oligosaccharide derivs. contg. glucuronic acid and glucosamine as sebum prodn. inhibitors for prevention or treatment of diseases caused by excessive prodn. of sebum)

IT Oligosaccharides, preparation
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of oligosaccharide derivs. contg. glucuronic acid and glucosamine as sebum prodn. inhibitors for prevention or treatment of diseases caused by excessive prodn. of sebum)

IT 247915-54-4P 247915-55-5P 247915-56-6P 247915-57-7P
RL: BAC (Biological activity or effector, except adverse); BPN

(Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of oligosaccharide derivs. contg. glucuronic acid and glucosamine as sebum prodn. inhibitors for prevention or treatment of diseases caused by excessive prodn. of sebum)

IT 247915-58-8P 247915-60-2P 249281-50-3P 249281-51-4P
331942-82-6P 331942-85-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of oligosaccharide derivs. contg. glucuronic acid and glucosamine as sebum prodn. inhibitors for prevention or treatment of diseases caused by excessive prodn. of sebum)

IT 9067-32-7, Sodium hyaluronate
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of oligosaccharide derivs. contg. glucuronic acid and glucosamine as sebum prodn. inhibitors for prevention or treatment of diseases caused by excessive prodn. of sebum)

IT 37259-53-3, Hyaluronidase
RL: CAT (Catalyst use); USES (Uses)
(prepn. of oligosaccharide derivs. contg. glucuronic acid and glucosamine as sebum prodn. inhibitors for prevention or treatment of diseases caused by excessive prodn. of sebum)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 16 MARPAT COPYRIGHT 2002 ACS
(ALL HITs ARE ITERATION INCOMPLETES)

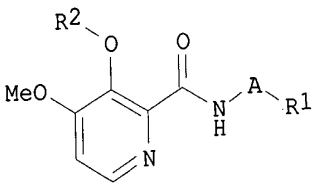
ACCESSION NUMBER: 134:56577 MARPAT
TITLE: Pyridinecarboxamides and their use as plant protection agents
INVENTOR(S): Backhaus, Dirk; Jordan, Stephan; Boie, Christiane; Schneider, Udo; Gayer, Herbert; Vaupel, Martin; Mauler-Machnik, Astrid; Wachendorff-Neumann, Ulrike; Kuck, Karl-Heinz
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076979	A1	20001221	WO 2000-EP4870	20000529

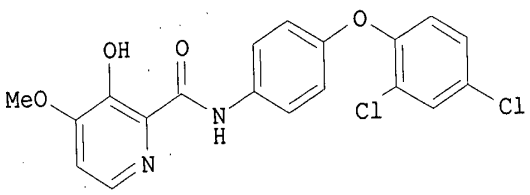
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
DE 19958166 A1 20001214 DE 1999-19958166 19991202
DE 1999-19926174 19990609
PRIORITY APPLN. INFO.: DE 1999-19958166 19991202

GI



I



II

AB Pyridinecarboxamides I [A = bond, (un)substituted alkylene, heteroalkylene; R1 = (un)substituted cycloalkyl, cycloalkenyl, aryl, heterocyclyl; R2 = H, acyl, alkoxycarbonyl] were prepd. for use as agricultural fungicides. Thus, the amide II was obtained by amidation. II was .gtoreq.91% effective against Botrytis on beans at 500 g/ha.

IC ICM C07D213-81
ICS C07D405-12; A01N043-40
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 5
ST pyridinecarboxamide prepn fungicide
IT Fungicides
(agrochem.; prepn. of pyridinecarboxamides as agricultural fungicides)
IT 313643-52-6P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of pyridinecarboxamides as agricultural fungicides)
IT 267415-65-6P 267415-77-0P 267415-79-2P 267415-86-1P
267416-59-1P 313643-53-7P 313643-54-8P 313643-55-9P
313643-56-0P 313643-57-1P 313643-58-2P 313643-59-3P
313643-60-6P 313643-61-7P 313643-62-8P 313643-63-9P
313643-64-0P 313643-65-1P 313643-66-2P 313643-67-3P
313643-68-4P 313643-69-5P 313643-70-8P 313643-71-9P
313643-72-0P 313643-73-1P 313643-74-2P 313643-75-3P
313643-76-4P 313643-77-5P 313643-78-6P 313643-79-7P
313643-80-0P 313643-81-1P 313643-82-2P 313643-83-3P
313643-84-4P 313643-85-5P 313643-86-6P 313643-87-7P

313643-88-8P 313643-89-9P 313643-90-2P 313643-91-3P
313643-92-4P 313643-93-5P 313643-94-6P 313643-95-7P
313643-96-8P
RL: AGR (Agricultural use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyridinecarboxamides as agricultural fungicides)
IT 14861-17-7, 4-(2,4-Dichlorophenoxy)aniline 210300-09-7, 3-Hydroxy-4-methoxy-2-pyridinecarboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyridinecarboxamides as agricultural fungicides)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 16 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 133:99567 MARPAT
TITLE: Glucuronate and glucosamine derivatives-containing compounds as leukocyte-vascular endothelial cell adhesion inhibitors
INVENTOR(S): Yatsuka, Nobuaki; Sato, Nobuyuki; Moriyama, Shigeru; Tamai, Tadakazu; Nishikawa, Masazumi
PATENT ASSIGNEE(S): Maruha Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000191538	A2	20000711	JP 1998-372864	19981228

AB Glucuronate and glucosamine derivs.-contg. compds. (Markush's structures given) are claimed as leukocyte-vascular endothelial cell adhesion inhibitors for treatment of ischemia-reperfusion injury and inflammatory diseases. Formulation examples of tablets, capsules, suspensions, suppositories, and injections were given.
IC ICM A61K031-7012
ICS A61K031-7028; A61P009-00; A61P029-00; A61P043-00; A61K031-715; C08B037-00; C07H007-033; C07H015-04
CC 1-8 (Pharmacology)
Section cross-reference(s): 33, 63
ST glucuronate glucosamine deriv leukocyte endothelium adhesion inhibitor; antiischemic glucuronate glucosamine deriv adhesion inhibitor; antiinflammatory glucuronate glucosamine deriv adhesion inhibitor
IT Drug delivery systems
(capsules; glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)
IT Adhesion, biological
Anti-inflammatory agents
Anti-ischemic agents
(glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)
IT Drug delivery systems
(injections; glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)
IT Reperfusion

(injury; glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)

IT Reperfusion
(ischemia injury; glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)

IT Heart, disease
(ischemia, -reperfusion injury; glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)

IT Drug delivery systems
(suppositories; glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)

IT Drug delivery systems
(suspensions; glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)

IT Drug delivery systems
(tablets; glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)

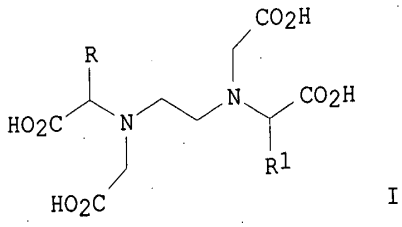
IT 187465-39-0P 187465-40-3P 198191-89-8P 198191-90-1P
198191-91-2P 198191-93-4P 198191-95-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)

IT 9067-32-7, Sodium hyaluronate 37259-53-3, Hyaluronidase
RL: RCT (Reactant); RACT (Reactant or reagent)
(glucuronate and glucosamine derivs.-contg. compds. as leukocyte-vascular endothelial cell adhesion inhibitors)

L15 ANSWER 6 OF 16 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 131:237141 MARPAT
TITLE: Manganese chelates with high relaxivity in serum
INVENTOR(S): Brochetta, Marino; Calabi, Luisella; Palano, Daniella; Paleari, Lino; Uggeri, Fulvio
PATENT ASSIGNEE(S): Bracco S.P.A., Italy; Dibra S.P.A.
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945967	A1	19990916	WO 1999-EP1490	19990308
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
IT 1298613	B1	20000112	IT 1998-MI476	19980310
EP 1061956	A1	20001227	EP 1999-910335	19990308
R: DE, FR, GB, IT				
JP 2002506049	T2	20020226	JP 2000-535380	19990308
US 6337064	B1	20020108	US 2000-601576	20000925
PRIORITY APPLN. INFO.:			IT 1998-MI476	19980310

GI



I

AB Racemic and optically active I [R and R1 are independently H or a linear/branched satd./unsatd. C1-20 alkyl chain, with the chain contg. .gtoreq. 1 N or as well as CO, CONH, NHCO, SO, SO2, SO2NH groups or with the chain contg. .gtoreq. 1 NH2, OH, halogen, CO2H groups and the resp. ester or amide derivs., or the chain contg. .gtoreq. R2 cyclic residues, which are the same or different, nonfused or fused] and their Mn complexes were prepd. and the relaxivity of the Mn complexes were detd. These complexes can be used and MRI imaging agents.

IC ICM A61K049-00
ICS C07C229-28; C07C229-36; C07C233-83; C07D209-20

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 8, 34, 77

ST manganese ethylenediaminetetraacetate complex prepn relaxivity imaging agent

IT Transition metal complexes
Transition metal complexes
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid, manganese; prepn. and relaxivity as imaging agents)

IT Imaging agents
(manganese ethylenediaminetetraacetate complexes)

IT Amino acids, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and complexation with manganese in prepn. of imaging agents)

IT Magnetic relaxation
(relaxivity of manganese ethylenediaminetetraacetate complexes)

IT Amino acids, preparation
Amino acids, preparation
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(transition metal complexes, manganese; prepn. and relaxivity as imaging agents)

IT 243964-95-6 243964-98-9 243965-01-7 243965-04-0 243965-07-3 243965-10-8 243965-13-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. and complexation with manganese as MRI imaging agents)

IT 243964-86-5P 243964-89-8P 243964-92-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

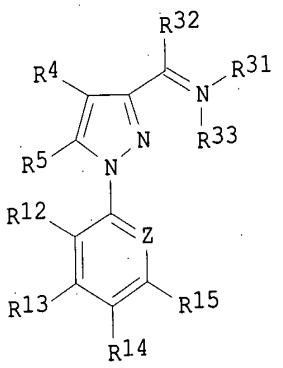
RACT (Reactant or reagent)
(prepn. and complexation with manganese as MRI imaging agents)
IT 243964-94-5P 243964-97-8P 243965-00-6P 243965-03-9P
243965-06-2P 243965-09-5P 243965-12-0P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. as NMR imaging agents)
IT 243964-85-4P 243964-88-7P 243964-91-2P
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. as NMR imaging agents and relaxivity)
IT 16874-17-2P, tert-Butyl L-phenylalaninate 119590-67-9P
203627-83-2P 203627-84-3P 243965-14-2P 243965-15-3P
243965-16-4P 243965-17-5P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(reactant for prepn. of manganese ethylenediaminetetraacetate complexes as MRI imaging agents)
IT 63-91-2, L-Phenylalanine, reactions 79-08-3, Bromoacetic acid
106-93-4, 1,2-Dibromoethane 107-15-3, 1,2-Ethanediamine, reactions
1041-01-6, O-(4-Hydroxyphenyl)-3,5-diiodo-L-tyrosine 5292-43-3,
tert-Butyl bromoacetate 6284-40-8, 1-Deoxy-1-(methylamino)-D-glucitol 7773-01-5, Manganese dichloride 17739-45-6,
2-(2-Bromoethoxy)tetrahydropyran 35016-63-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant for prepn. of manganese ethylenediaminetetraacetate complexes as MRI imaging agents)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 16 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 130:52416 MARPAT
TITLE: Pesticidal 1-aryl-3-iminopyrazoles
INVENTOR(S): Manning, David Treadway; Wu, Tai-teh
PATENT ASSIGNEE(S): Rhone-Poulenc Agro, Fr.
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856767	A1	19981217	WO 1998-EP1764	19980309
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9801934	A	19990906	ZA 1998-1934	19980306
AU 9870415	A1	19981230	AU 1998-70415	19980309
AU 745011	B2	20020307		
US 5965491	A	19991012	US 1998-36794	19980309

BR 9808019	A	20000308	BR 1998-8019	19980309
EP 1007513	A1	20000614	EP 1998-917082	19980309
R: AT, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001518936	T2	20011016	JP 1998-546387	19980309
NO 9904355	A	19991110	NO 1999-4355	19990908
PRIORITY APPLN. INFO.:			US 1997-40135P	19970310
			WO 1998-EP1764	19980309

GI



I

AB The title compds. [I; R31 = H, CN, NO2, etc.; R32 = C1-6 alkyl, C3-7 cycloalkyl, etc.; R33 = a lone pair of electrons, O, S, etc.; R4 = C1-6 alkyl, C3-6 cycloalkyl, C4-8 (cycloalkyl)alkyl, etc.; R5 = H, halo, CN, etc.; Z = N, CH, C(halo), etc.; R12-R15 = H, halo, CN, etc.], useful as pesticides, esp. for controlling arthropods, or as intermediates to other pesticides, were prepd. Thus, reaction of 3-acetyl-5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-methylsulfinyl-1H-pyrazole with aniline in the presence of p-TsOH in C6H6 afforded I [R32 = Me; R31 = Ph; R33 = a lone pair of electrons; R4 = MeS(O); R5 = NH2; R12 = Cl, R13 = R15 = H; R14 = CF3; Z = C(Cl)] which showed high systemic activity on aphids and on greenbugs.

IC ICM C07D231-44
ICS A01N043-56; C07D405-12; C07D401-12; C07D403-12; C07D417-12

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5

ST aryliminopyrazole prepn pesticide arthropod

IT Arthropod (Arthropoda)
Pesticides
(pesticidal 1-aryl-3-iminopyrazoles)

IT 217435-97-7P	217435-98-8P	217435-99-9P	217436-00-5P
217436-01-6P	217436-02-7P	217436-03-8P	217436-04-9P
217436-05-0P	217436-06-1P	217436-07-2P	217436-08-3P
217436-09-4P	217436-10-7P	217436-11-8P	217436-12-9P
217436-13-0P	217436-14-1P	217436-15-2P	217436-16-3P
217436-17-4P	217436-18-5P	217436-19-6P	217436-20-9P
217436-21-0P	217436-22-1P	217436-23-2P	217436-24-3P
217436-25-4P	217436-26-5P	217436-27-6P	217436-28-7P
217436-29-8P	217436-30-1P	217436-31-2P	217436-32-3P
217436-33-4P	217436-34-5P	217436-35-6P	217436-37-8P
217436-38-9P	217436-40-3P	217436-42-5P	217436-44-7P

217436-45-8P 217436-47-0P 217436-49-2P 217436-50-5P
217436-51-6P 217436-52-7P 217436-53-8P 217436-54-9P
217436-55-0P 217436-56-1P 217436-57-2P 217436-58-3P
217436-59-4P 217436-60-7P 217436-62-9P 217436-64-1P
217436-66-3P 217436-68-5P 217436-69-6P 217436-70-9P
217436-71-0P 217436-72-1P 217436-73-2P 217436-74-3P
217436-75-4P 217436-76-5P 217436-77-6P 217436-78-7P
217436-79-8P 217436-81-2P 217436-82-3P 217436-83-4P
217436-84-5P 217436-85-6P 217436-86-7P 217436-87-8P
217436-88-9P 217436-89-0P 217436-90-3P 217436-91-4P
217436-92-5P 217436-93-6P 217436-94-7P 217436-95-8P
217436-96-9P 217436-97-0P 217436-98-1P 217436-99-2P
217437-00-8P 217437-01-9P 217437-02-0P 217437-03-1P
217437-04-2P 217437-05-3P 217437-06-4P 217437-07-5P
217437-08-6P 217437-09-7P 217437-10-0P 217437-11-1P
217437-12-2P 217437-13-3P 217437-14-4P 217437-15-5P
217437-16-6P 217437-17-7P 217437-18-8P 217437-19-9P
217437-20-2P 217437-21-3P 217437-22-4P 217437-23-5P
217437-24-6P 217437-25-7P 217437-26-8P 217437-27-9P
217437-28-0P 217437-29-1P 217437-30-4P 217437-31-5P
217437-32-6P 217437-33-7P 217437-34-8P 217437-35-9P
217437-36-0P 217437-37-1P 217437-38-2P 217437-39-3P
217437-40-6P 217437-41-7P 217437-42-8P 217437-43-9P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pesticidal 1-aryl-3-iminopyrazoles)

IT 62-53-3, Aniline, reactions 554-00-7, 2,4-Dichloroaniline
209861-58-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(pesticidal 1-aryl-3-iminopyrazoles)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 16 MARPAT COPYRIGHT 2002 ACS
(ALL HITs ARE ITERATION INCOMPLETES)
ACCESSION NUMBER: 130:29064 MARPAT
TITLE: Composition for dyeing keratin fibers comprising a pyrazolin-4,5-dione and an aromatic primary amine
INVENTOR(S): Vidal, Laurent; Malle, Gerard; Maubru, Mireille
PATENT ASSIGNEE(S): L'Oreal, Fr.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851268	A1	19981119	WO 1998-FR619	19980326

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

FR 2763241	A1	19981120	FR 1997-5843	19970513
FR 2763241	B1	19990702		
AU 9870521	A1	19981208	AU 1998-70521	19980326
EP 981320	A1	20000301	EP 1998-917247	19980326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000512314	T2	20000919	JP 1998-548850	19980326
US 2002040508	A1	20020411	US 1999-423521	19991110
PRIORITY APPLN. INFO.:			FR 1997-5843	19970513
			WO 1998-FR619	19980326

AB A compn. for dyeing keratin fibers, in particular human keratin fibers such as hair comprising at least one pyrazolin-4,5-dione (Markush structure given) and at least one arom. primary amine. Said compn. enables the dyeing of keratin fibers without an oxidizing agent in shades which are strong, varied, resistant and less selective than those of prior art. The invention also concerns dyeing methods and devices using said compn. A hair dye compn. contained 3-methyl-1-phenylpyrazolin-4,5-dione 0.940, paraphenylenedimaine 0.540, Et alc. 40.0, citric acid q.s. pH = 2, and water q.s. 100.0 g.

IC ICM A61K007-13
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 28
ST hair dye pyrazolindione arom amine

IT Amines, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study);
USES (Uses)
(arom.; compn. for dyeing keratin fibers comprising pyrazolindione and arom. primary amine)

IT Alcohols, biological studies
Glycols, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study);
USES (Uses)
(compn. for dyeing keratin fibers comprising pyrazolindione and arom. primary amine)

IT Hair preparations
(dyes; compn. for dyeing keratin fibers comprising pyrazolindione and arom. primary amine)

IT Glycols, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study);
USES (Uses)
(ethers; compn. for dyeing keratin fibers comprising pyrazolindione and arom. primary amine)

IT Ethers, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study);
USES (Uses)
(glycol; compn. for dyeing keratin fibers comprising pyrazolindione and arom. primary amine)

IT Solvents
(org.; compn. for dyeing keratin fibers comprising pyrazolindione and arom. primary amine)

IT 62-53-3D, Aniline, derivs. 95-55-6 95-70-5 106-50-3, 1,4-Benzenediamine, biological studies 123-30-8 399-95-1

452-58-4, 2,3-Pyridinediamine 615-66-7 881-05-0 1004-76-8
1630-11-1 2835-96-3 2835-98-5 2835-99-6 3240-72-0
4592-60-3 4734-73-0 5306-96-7 13795-02-3 16461-98-6,
1H-Pyrazole-3,4-diamine 17672-22-9 29785-47-5 45514-38-3
49714-81-0 51942-09-7 52605-79-5 59056-57-4 62349-56-8
62349-59-1 63886-74-8 66566-48-1 66583-86-6 69151-32-2
76368-87-1 79352-72-0 93841-24-8 96886-30-5 97902-52-8
104333-09-7 110952-46-0 126335-43-1 129697-50-3 155601-16-4
160950-38-9 168202-61-7 184172-86-9 184172-97-2 184172-99-4
184173-43-1 197651-70-0 197651-76-6 197651-78-8 197651-80-2
197651-86-8 197651-88-0 197651-92-6 197651-94-8 197651-95-9
197651-97-1 197651-99-3 197652-01-0 197652-03-2 197652-05-4
197652-07-6 197652-14-5 197652-16-7 197652-18-9 197652-20-3
197652-22-5 197652-24-7 197652-26-9 197652-28-1 197652-30-5
197652-32-7 197652-34-9 197652-36-1 197652-39-4 199340-99-3
201599-07-7 201599-12-4, Pyrazolo[1,5-a]pyrimidine-3,7-diamine
207568-58-9 216319-92-5 216320-73-9 216320-74-0 216320-76-2
216320-78-4 216320-80-8 216320-82-0 216320-84-2 216320-85-3
216320-86-4 216320-87-5 216321-12-9
RL: BUU (Biological use, unclassified); BIOL (Biological study);
USES (Uses)
(compn. for dyeing keratin fibers comprising pyrazolindione and arom. primary amine)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

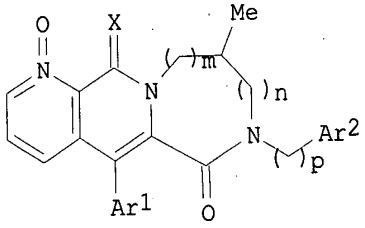
L15 ANSWER 9 OF 16 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 129:95515 MARPAT
TITLE: Preparation of medium-ring polycyclic heterocycles as tachykinin receptor antagonists
INVENTOR(S): Natsugari, Hideaki; Ishimaru, Takenori; Doi, Takayuki; Ikeura, Yoshinori; Kimura, Chiharu; Tarui, Naoki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: U.S., 66 pp., Cont.-in-part of U.S. Ser. No. 621,360.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5770590	A	19980623	US 1996-717801	19960923
JP 09263585	A2	19971007	JP 1996-66337	19960322
JP 2976097	B2	19991110		
JP 09263587	A2	19971007	JP 1997-20386	19960322
CN 1140172	A	19970115	CN 1996-106081	19960323
US 5786352	A	19980728	US 1996-621360	19960325
US 6147071	A	20001114	US 1998-87894	19980601
			JP 1995-91436	19950324
			JP 1995-207553	19950720
			JP 1995-264727	19950918
			JP 1996-30033	19960123
			JP 1996-66337	19960322
			US 1996-621360	19960325

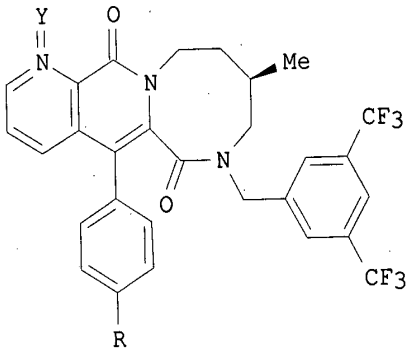
PRIORITY APPLN. INFO.:

JP 1996-214698 19960814

GI



I



II

AB A variety of polycyclic heterocycles are disclosed, and in particular the compds. I and salts are claimed [wherein X = O, S; Ar1, Ar2 = certain (un)substituted Ph; m, n = 0 to 4; (m+n) = 2 to 4; p = 1 to 6]. The compds. show an excellent tachykinin receptor antagonistic effect. For instance, (9R)-7-[3,5-bis(trifluoromethyl)benzyl]-6,7,8,9,10,11-hexahydro-9-methyl-5-(4-methylphenyl)-6,13-dioxo-13H-[1,4]diazocino[2,1-g][1,7]naphthyridine, i.e., II [Y = absent, R = Me] (prepn. given) underwent hydroxylation by Streptomyces subrutilus IFO 13388 to give II [Y = absent, R = CH2OH] (III). The latter underwent acetylation with Ac2O and pyridine, N-oxidn. with m-ClC6H4C(O)OOH, and hydrolytic deacetylation, to give title compd. II [Y = O, R = CH2OH]. III had an ID50 of 2.5 .mu.g/kg i.v. for inhibiting capsaicin-induced tracheal plasma extravasation in anesthetized guinea pigs. I also showed substance P receptor antagonistic and NK2 receptor inhibitory activities.

IC ICM A61K031-33
ICS A61K031-55; C07D245-00; C07D487-00

NCL 514183000

CC 28-22 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST heterocyclic prepn tachykinin receptor antagonist; diazocinonaphthyridine prepn substance P receptor antagonist

IT Tachykinin receptors
(NK1 antagonists; prepn. of medium-ring polycyclic heterocycles as tachykinin receptor antagonists)

IT Tachykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NK1, treatment of mediated diseases; prepn. of medium-ring polycyclic heterocycles as tachykinin receptor antagonists)

IT Tachykinin receptors
(NK2 antagonists; prepn. of medium-ring polycyclic heterocycles as tachykinin receptor antagonists)

IT Tachykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NK2, treatment of mediated diseases; prepn. of medium-ring polycyclic heterocycles as tachykinin receptor antagonists)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(treatment of mediated diseases; prepn. of medium-ring polycyclic heterocycles as tachykinin receptor antagonists)

IT 207606-22-2P 207606-26-6P
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of medium-ring polycyclic heterocycles as tachykinin receptor antagonists)

IT 183145-60-0P 183549-77-1P 183549-78-2P 183549-79-3P
183549-80-6P 183549-81-7P 183549-82-8P 183549-83-9P
183549-84-0P 183549-85-1P 183549-86-2P 183549-87-3P
183549-88-4P 183549-89-5P 183549-90-8P 183549-91-9P
183549-92-0P 183549-93-1P 183549-94-2P 183549-95-3P
183549-96-4P 183549-97-5P 183549-98-6P 183550-00-7P
183550-02-9P 183550-03-0P 183550-05-2P 183550-07-4P
183550-08-5P 183550-09-6P 183550-10-9P 183550-11-0P
183550-13-2P 183550-15-4P 183550-16-5P 183550-18-7P
183550-20-1P 183550-21-2P 183550-23-4P 183550-26-7P
183550-27-8P 183550-29-0P 183550-31-4P 183550-32-5P
183550-33-6P 183550-34-7P 183550-35-8P 183550-36-9P
183550-37-0P 183550-38-1P 183550-39-2P 183550-40-5P
183550-41-6P 183550-42-7P 183550-43-8P 183550-44-9P
183550-45-0P 183550-46-1P 183550-47-2P 183550-48-3P
183550-49-4P 183550-50-7P 183550-51-8P 183550-52-9P
183550-53-0P 183550-54-1P 183550-55-2P 183550-56-3P
183550-57-4P 183550-58-5P 183550-59-6P 183550-60-9P
183550-61-0P 183550-62-1P 183550-63-2P 183550-64-3P
183550-65-4P 183550-66-5P 183550-67-6P 183550-68-7P
183550-69-8P 183550-70-1P 207606-24-4P 207606-31-3P
207606-34-6P 209672-70-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of medium-ring polycyclic heterocycles as tachykinin receptor antagonists)

IT 67-63-0, Isopropanol, reactions 100-46-9, Benzylamine, reactions
102-49-8, 3,4-Dichlorobenzylamine 104-63-2, N-(2-Hydroxyethyl)benzenemethanamine 106-38-7, 4-Bromotoluene
109-01-3, 1-Methylpiperazine 109-73-9, n-Butylamine, reactions
110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions

156-87-6, 3-Amino-1-propanol 616-30-8, 3-Amino-1,2-propanediol
628-87-5, Iminodiacetonitrile 685-87-0, Diethyl bromomalonate
699-98-9, Pyridine-2,3-dicarboxylic acid anhydride 765-30-0,
Cyclopropylamine 2508-29-4, 5-Amino-1-pentanol 5003-71-4
6850-57-3, 2-Methoxybenzylamine 13325-10-5, 4-Amino-1-butanol
13937-08-1, Diethyl hydroxymalonate 14505-28-3 18638-99-8,
3,4,5-Trimethoxybenzylamine 24687-79-4 32247-96-4,
3,5-Bis(trifluoromethyl)benzyl bromide 34967-24-3,
3,5-Dimethoxybenzylamine 40172-02-9 40172-06-3 44565-27-7,
4-Amino-2-methyl-1-butanol 64362-32-9, 3-Benzoyl-2-
pyridinecarboxylic acid 74975-27-2, 4-(4-Methylbenzoyl)-3-
pyridinecarboxylic acid 80657-57-4 85068-29-7,
3,5-Bis(trifluoromethyl)benzylamine 88586-62-3,
(S)-3-Amino-2-methyl-1-propanol 104154-93-0 110239-06-0, Diethyl
4-phenyl-2,3-pyridinedicarboxylate 147078-78-2,
2-Chloro-4-phenyl-3-pyridinecarboxylic acid 183551-51-1,
3,5-Bis(trifluoromethyl)benzyl methanesulfonate 183551-52-2
183551-53-3 183551-54-4 183551-55-5 183551-69-1 183551-70-4
183551-71-5 183812-31-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of medium-ring polycyclic heterocycles as tachykinin
receptor antagonists)

IT 110171-23-8P 116060-91-4P 147078-85-1P 156241-24-6P
183550-71-2P 183550-72-3P 183550-73-4P 183550-74-5P
183550-75-6P 183550-76-7P 183550-77-8P 183550-78-9P
183550-79-0P 183550-80-3P 183550-81-4P 183550-82-5P
183550-83-6P 183550-84-7P 183550-85-8P 183550-86-9P
183550-87-0P 183550-88-1P 183550-89-2P 183550-90-5P
183550-91-6P 183550-92-7P 183550-93-8P 183550-94-9P
183550-95-0P 183550-96-1P 183550-97-2P 183550-98-3P
183550-99-4P 183551-00-0P 183551-01-1P 183551-02-2P
183551-03-3P 183551-04-4P 183551-05-5P 183551-06-6P
183551-07-7P 183551-08-8P 183551-09-9P 183551-10-2P
183551-11-3P 183551-12-4P 183551-13-5P 183551-14-6P
183551-15-7P 183551-16-8P 183551-17-9P 183551-18-0P
183551-19-1P 183551-20-4P 183551-21-5P 183551-22-6P
183551-23-7P 183551-24-8P 183551-25-9P 183551-26-0P
183551-27-1P 183551-28-2P 183551-29-3P 183551-30-6P
183551-31-7P 183551-32-8P 183551-33-9P 183551-34-0P
183551-35-1P 183551-36-2P 183551-37-3P 183551-38-4P
183551-39-5P 183551-40-8P 183551-41-9P 183551-42-0P
183551-43-1P 183551-44-2P 183551-45-3P 183551-46-4P
183551-47-5P 183551-48-6P 183551-49-7P 183551-50-0P
183551-56-6P 183551-57-7P 183551-58-8P 183551-59-9P
183551-60-2P 183551-61-3P 183551-62-4P 183551-63-5P
183551-64-6P 183551-65-7P 183551-66-8P 183551-67-9P
183551-68-0P 183551-72-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(prepn. of medium-ring polycyclic heterocycles as tachykinin
receptor antagonists)

IT 33507-63-0, Substance P
RL: BPR (Biological process); BSU (Biological study, unclassified);
MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(treatment of mediated diseases; prepn. of medium-ring polycyclic
heterocycles as tachykinin receptor antagonists)

L15 ANSWER 10 OF 16 MARPAT COPYRIGHT 2002 ACS

(ALL HITs ARE ITERATION INCOMPLETES)

ACCESSION NUMBER: 126:263939 MARPAT

TITLE: Preparation of acylaminosalicylamides as pesticides

INVENTOR(S): Seitz, Thomas; Naumann, Klaus; Tiemann, Ralf; Stenzel, Klaus; Haenssler, Gerd; Dutzmann, Stefan

PATENT ASSIGNEE(S): Bayer A.-G., Germany; Seitz, Thomas; Naumann, Klaus; Tiemann, Ralf; Stenzel, Klaus; Haenssler, Gerd; Dutzmann, Stefan

SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9708135	A1	19970306	WO 1996-EP3637	19960819
W: AU, BB, BG, BR, BY, CA, CN, CZ, HU, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, TR, UA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19626311	A1	19971023	DE 1996-19626311	19960701
AU 9668740	A1	19970319	AU 1996-68740	19960819
EP 848700	A1	19980624	EP 1996-929273	19960819
R: BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, PT, IE				
CN 1200725	A	19981202	CN 1996-197825	19960819
BR 9610048	A	19990706	BR 1996-10048	19960819
JP 11511442	T2	19991005	JP 1996-509794	19960819
TW 379212	B	20000111	TW 1996-85110382	19960827
ZA 9607317	A	19970303	ZA 1996-7317	19960829
US 6001879	A	19991214	US 1998-29110	19980218
PRIORITY APPLN. INFO.:			DE 1995-19531891	19950830
			DE 1996-19615453	19960419
			DE 1996-19626311	19960701
			WO 1996-EP3637	19960819

AB R1CONHZ1CONHZ2R2 (Z1 = 2-hydroxy-1,3-phenylene)[I; R1 = H, alkyl, alkoxy; R2 = cycloalk(en)yl, heterocyclyl, aryl; Z2 = bond or alkylene] were prepd. Thus, 3-nitrosalicylic acid was amidated by 4-PhC6H4NH2 and the product treated with HCO2H/Pd to give I (R1 = H, R2 = 4-biphenylyl, Z2 = bond). Data for biol. activity of I were given.

IC ICM C07C237-44
ICS C07C235-58; C07C235-64; C07C235-62; A01N037-18; A01N037-24

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 5

ST salicylamide acylamino prepn pesticide

IT Fungicides
(agrochem.; prepn. of acylaminosalicylamides as pesticides)

IT Antibacterial agents
Insecticides
Pesticides
(prepn. of acylaminosalicylamides as pesticides)

IT 34999-29-6P 34999-30-9P 124071-02-9P 148174-05-4P
148174-07-6P 188746-37-4P 188746-39-6P 188746-40-9P

188746-41-0P 188746-42-1P 188746-43-2P 188746-44-3P
188746-45-4P 188746-46-5P 188746-47-6P 188746-48-7P
188746-49-8P 188746-50-1P 188755-75-1P 188755-76-2P
188755-77-3P 188755-78-4P 188755-79-5P 188755-80-8P
188755-81-9P 188755-82-0P 188755-83-1P 188755-84-2P
188755-85-3P 188755-86-4P 188755-87-5P 188755-88-6P
188755-89-7P 188755-90-0P 188755-91-1P 188755-92-2P
188755-93-3P 188755-94-4P 188755-95-5P 188755-96-6P
188755-97-7P 188755-98-8P 188755-99-9P 188756-00-5P
188756-01-6P 188756-02-7P 188756-03-8P 188756-04-9P
188756-05-0P 188756-06-1P 188756-07-2P 188756-08-3P
188756-10-7P 188756-11-8P 188756-12-9P 188756-13-0P
188756-14-1P 188756-15-2P 188756-16-3P 188756-17-4P
188756-18-5P 188756-19-6P 188756-20-9P 188756-21-0P
188756-22-1P 188756-23-2P 188756-24-3P 188756-25-4P
188756-26-5P 188756-27-6P 188756-30-1P 188756-33-4P
188756-34-5P 188756-35-6P 188756-36-7P 188756-37-8P
188756-38-9P 188756-39-0P 188756-40-3P 188756-41-4P
188756-42-5P 188756-43-6P 188756-44-7P 188756-45-8P
188756-46-9P 188756-47-0P 188756-48-1P 188756-49-2P
188756-50-5P 188756-51-6P 188756-52-7P 188756-53-8P
188756-54-9P 188756-55-0P 188756-56-1P 188756-57-2P
188756-58-3P 188756-59-4P 188756-60-7P 188756-61-8P
188756-62-9P 188756-63-0P 188756-64-1P 188756-65-2P
188756-66-3P 188756-67-4P 188756-68-5P 188756-69-6P
188756-70-9P 188756-71-0P 188756-72-1P 188756-73-2P
188756-74-3P 188756-75-4P 188756-76-5P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acylaminosalicylamides as pesticides)

IT 85-38-1, 3-Nitrosalicylic acid 92-67-1, 4-Aminobiphenyl 403-40-7, 1-(4-Fluorophenyl)ethylamine 107558-95-2, 2-Benzyloxy-3-nitrobenzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of acylaminosalicylamides as pesticides)

IT 188756-77-6P 188756-78-7P 188756-79-8P 188756-80-1P
188756-81-2P 188756-82-3P 188756-83-4P 188756-84-5P
188756-85-6P 188756-86-7P 188756-87-8P 188756-88-9P
188756-89-0P 188756-90-3P 188756-91-4P 188756-92-5P
188756-93-6P 188756-94-7P 188756-95-8P 188756-96-9P
188756-97-0P 188756-98-1P 188756-99-2P 188757-00-8P
188757-01-9P 188757-02-0P 188757-03-1P 188757-04-2P
188757-05-3P 188757-06-4P 188757-07-5P 188757-08-6P
188757-09-7P 188757-10-0P 188757-11-1P 188757-12-2P
188757-13-3P 188757-14-4P 188757-15-5P 188757-16-6P
188757-17-7P 188757-18-8P 188757-19-9P 188757-20-2P
188757-21-3P 188757-22-4P 188757-23-5P 188757-24-6P
188757-25-7P 188757-26-8P 188757-27-9P 188757-28-0P
188757-29-1P 188757-30-4P 188757-31-5P 188757-32-6P
188757-33-7P 188757-34-8P 188757-35-9P 188757-36-0P
188757-37-1P 188757-38-2P 188757-39-3P 188757-40-6P
188757-41-7P 188757-42-8P 188757-43-9P 188757-44-0P
188757-45-1P 188757-46-2P 188757-47-3P 188757-48-4P
188757-49-5P 188757-50-8P 188757-51-9P 188757-52-0P
188757-53-1P 188757-54-2P 188757-55-3P 188757-56-4P
188757-57-5P 188757-58-6P 188757-59-7P 188757-60-0P

188757-61-1P	188757-62-2P	188757-63-3P	188757-64-4P
188757-65-5P	188757-66-6P	188757-67-7P	188757-68-8P
188757-69-9P	188757-70-2P	188757-71-3P	188757-72-4P
188757-73-5P	188757-74-6P	188757-75-7P	188757-76-8P
188757-77-9P	188757-78-0P	188757-79-1P	188757-80-4P
188757-81-5P	188757-82-6P	188757-83-7P	188757-84-8P
188757-85-9P	188757-86-0P	188757-87-1P	188757-88-2P
188757-89-3P	188757-90-6P	188757-91-7P	188757-92-8P
188757-93-9P	188757-94-0P	188757-95-1P	188757-96-2P
188757-97-3P	188757-98-4P	188758-00-1P	188758-01-2P
188758-02-3P	188758-03-4P	188758-04-5P	188758-05-6P
188758-06-7P	188758-07-8P	188758-08-9P	188758-09-0P
188758-10-3P	188758-11-4P	188758-12-5P	188758-13-6P
188758-14-7P	188758-15-8P	188758-16-9P	188758-17-0P
188758-18-1P	188758-19-2P	188758-20-5P	188758-21-6P
188758-22-7P	188758-23-8P	188758-24-9P	188758-25-0P
188758-26-1P	188758-27-2P	188758-28-3P	188758-29-4P
188758-30-7P	188758-31-8P	188758-32-9P	188758-33-0P
188758-34-1P	188758-35-2P	188758-36-3P	188758-37-4P
188758-38-5P	188758-39-6P	188758-40-9P	188758-41-0P
188758-42-1P	188758-43-2P		

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of acylaminosalicylamides as pesticides)

L15 ANSWER 11 OF 16 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 126:8145 MARPAT
TITLE: Preparation of polycyclic heterocycles as tachykinin receptor antagonists
INVENTOR(S): Natsugari, Hideaki; Ishimaru, Takenori; Doi, Takayuki; Ikeura, Yoshinori; Kimura, Chiharu
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 94 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 733632	A1	19960925	EP 1996-104500	19960321
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9601160	A	19960925	NO 1996-1160	19960321
TW 394773	B	20000621	TW 1996-85103427	19960321
CA 2172421	AA	19960925	CA 1996-2172421	19960322
AU 9648261	A1	19961003	AU 1996-48261	19960322
AU 699611	B2	19981210		
CN 1140172	A	19970115	CN 1996-106081	19960323
IL 117631	A1	20001121	IL 1996-117631	19960324
BR 9601125	A	19980106	BR 1996-1125	19960325
PRIORITY APPLN. INFO.:			JP 1995-91436	19950324
			JP 1995-207553	19950720
			JP 1995-264727	19950918
			JP 1996-30033	19960123

GI For diagram(s), see printed CA Issue.
AB Title compds. [I; R = (CH2)nR4; R1,R2 = H or a substituent; R1R2 =

atoms to complete a (hetero)cyclic ring; ring B = heterocyclic ring; R3,R4 = (hetero)cyclic ring; X-Y = N:C, C(O)N, C(S)N; n = 1-6] were prepd. Thus, 4-BrC6H4Me was condensed with 2,3-pyridinedicarboxylic acid and the product amidated by HN(CH2CN)2 to give, after cyclization in 5 addnl. steps, 7-[3,5-bis(trifluoromethyl)benzyl]-6,7,8,9-tetrahydro-5-(4-methylphenyl)-6,11-dioxo-11H-pyrazino[2,1-g][1,7]naphthyridine. Data for in vitro biol. activity of selected I were given.

IC ICM C07D471-14
ICS A61K031-495; C07D498-04; C07D471-04; C07D487-04

CC 28-22 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST heterocyclic prepn tachykinin receptor antagonist

IT Tachykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NK2, mediated diseases; treatment; prepn. of polycyclic heterocycles as tachykinin receptor antagonists)

IT Tachykinin receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(mediated diseases; treatment; prepn. of polycyclic heterocycles as tachykinin receptor antagonists)

IT 33507-63-0, Substance P
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mediated diseases; treatment; prepn. of polycyclic heterocycles as tachykinin receptor antagonists)

IT 183145-60-0P 183549-77-1P 183549-78-2P 183549-79-3P
183549-80-6P 183549-81-7P 183549-82-8P 183549-83-9P
183549-84-0P 183549-85-1P 183549-86-2P 183549-87-3P
183549-88-4P 183549-89-5P 183549-90-8P 183549-91-9P
183549-92-0P 183549-93-1P 183549-94-2P 183549-95-3P
183549-96-4P 183549-97-5P 183549-98-6P 183550-00-7P
183550-02-9P 183550-03-0P 183550-05-2P 183550-07-4P
183550-08-5P 183550-09-6P 183550-10-9P 183550-11-0P
183550-13-2P 183550-15-4P 183550-16-5P 183550-18-7P
183550-20-1P 183550-21-2P 183550-23-4P 183550-26-7P
183550-27-8P 183550-29-0P 183550-31-4P 183550-32-5P
183550-33-6P 183550-34-7P 183550-35-8P 183550-36-9P
183550-37-0P 183550-38-1P 183550-39-2P 183550-40-5P
183550-41-6P 183550-42-7P 183550-43-8P 183550-44-9P
183550-45-0P 183550-46-1P 183550-47-2P 183550-48-3P
183550-49-4P 183550-50-7P 183550-51-8P 183550-52-9P
183550-53-0P 183550-54-1P 183550-55-2P 183550-56-3P
183550-57-4P 183550-58-5P 183550-59-6P 183550-60-9P
183550-61-0P 183550-62-1P 183550-63-2P 183550-64-3P
183550-65-4P 183550-66-5P 183550-67-6P 183550-68-7P
183550-69-8P 183550-70-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of polycyclic heterocycles as tachykinin receptor antagonists)

IT 67-63-0, Isopropanol, reactions 100-46-9, Benzylamine, reactions
102-49-8, 3,4-DichloroBenzylamine 104-63-2, N-(2-Hydroxyethyl)benzenemethanamine 106-38-7, 4-Bromotoluene

109-01-3, 1-Methylpiperazine 109-73-9, n-Butylamine, reactions
110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions
156-87-6, 3-Amino-1-propanol 616-30-8, 3-Amino-1,2-propanediol
628-87-5, Iminodiacetonitrile 685-87-0, Diethyl bromomalonate
699-98-9, Pyridine-2,3-dicarboxylic acid anhydride 765-30-0,
Cyclopropylamine 2508-29-4, 5-Amino-1-pentanol 5003-71-4
6850-57-3, 2-Methoxybenzylamine 13325-10-5, 4-Amino-1-butanol
13937-08-1, Diethyl hydroxymalonate 14505-28-3 18638-99-8,
3,4,5-Trimethoxybenzylamine 24687-79-4 32247-96-4,
3,5-Bis(trifluoromethyl)benzyl bromide 34967-24-3,
3,5-Dimethoxybenzylamine 40172-02-9 40172-06-3 44565-27-7,
4-Amino-2-methyl-1-butanol 64362-32-9, 3-Benzoyl-2-
pyridinecarboxylic acid 74975-27-2, 4-(4-Methylbenzoyl)-3-
pyridinecarboxylic acid 85068-29-7, 3,5-
Bis(trifluoromethyl)benzylamine 88586-62-3, (S)-3-Amino-2-methyl-1-
propanol 104154-93-0 110239-06-0, Diethyl 4-phenyl-2,3-
pyridinedicarboxylate 147078-78-2, 2-Chloro-4-phenyl-3-
pyridinecarboxylic acid 183551-51-1, 3,5-
Bis(trifluoromethyl)benzyl methanesulfonate 183551-52-2
183551-53-3 183551-54-4 183551-55-5 183551-69-1 183551-70-4
183551-71-5 183812-31-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of polycyclic heterocycles as tachykinin receptor
antagonists)

IT 116060-91-4P 147078-85-1P 156241-24-6P 183550-71-2P
183550-72-3P 183550-73-4P 183550-74-5P 183550-75-6P
183550-76-7P 183550-77-8P 183550-78-9P 183550-79-0P
183550-80-3P 183550-81-4P 183550-82-5P 183550-83-6P
183550-84-7P 183550-85-8P 183550-86-9P 183550-87-0P
183550-88-1P 183550-89-2P 183550-90-5P 183550-91-6P
183550-92-7P 183550-93-8P 183550-94-9P 183550-95-0P
183550-96-1P 183550-97-2P 183550-98-3P 183550-99-4P
183551-00-0P 183551-01-1P 183551-02-2P 183551-03-3P
183551-04-4P 183551-05-5P 183551-06-6P 183551-07-7P
183551-08-8P 183551-09-9P 183551-10-2P 183551-11-3P
183551-12-4P 183551-13-5P 183551-14-6P 183551-15-7P
183551-16-8P 183551-17-9P 183551-18-0P 183551-19-1P
183551-20-4P 183551-21-5P 183551-22-6P 183551-23-7P
183551-24-8P 183551-25-9P 183551-26-0P 183551-27-1P
183551-28-2P 183551-29-3P 183551-30-6P 183551-31-7P
183551-32-8P 183551-33-9P 183551-34-0P 183551-35-1P
183551-36-2P 183551-37-3P 183551-38-4P 183551-39-5P
183551-40-8P 183551-41-9P 183551-42-0P 183551-43-1P
183551-44-2P 183551-45-3P 183551-46-4P 183551-47-5P
183551-48-6P 183551-49-7P 183551-50-0P 183551-56-6P
183551-57-7P 183551-58-8P 183551-59-9P 183551-60-2P
183551-61-3P 183551-62-4P 183551-63-5P 183551-64-6P
183551-65-7P 183551-66-8P 183551-67-9P 183551-68-0P
183551-72-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(prepn. of polycyclic heterocycles as tachykinin receptor
antagonists)

L15 ANSWER 12 OF 16 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 122:315043 MARPAT
TITLE: Dermatan sulfate for anticoagulant and
intermediate for its preparation

INVENTOR(S): Ogawa, Tomoya; Goto, Fumitaka; Namikawa, Junichi
PATENT ASSIGNEE(S): Rikagaku Kenkyusho, Japan; Otsuka Pharma Co Ltd
SOURCE: Jpn. Kokai Tokkyo Koho, 36 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06256401	A2	19940913	JP 1993-62504	19930301

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title oligosaccharides (I; R = H; M = H, metal atom) are prepd. via intermediates, e.g., 2-deoxyazidogalactose derivs. [II; R1 = H, allyl, CH2Ph, C(:NH)CCl3; R2 = acyl group capable of leaving under a mild condition] and idose derivs. [III; R3 = OH, allyloxy, MeS, OC(:NH)CCl3; R4 = H, Ac, pivaloyl, toluoyl, allyl; R5 = H, Ac, CH2Ph, Me3Si, acyl group capable of leaving under a mild condition; R6 = H, Ac, p-methoxyphenyl; R5R6 forms an acetal group]. The process described gives in a large quantity dermatan sulfate I, which is expected to be useful as an anticoagulant (no data). Thus, 6.5 mg .beta.-I (R = CH2Ph, M = Na) was stirred with 10 mg 10% Pd-C in aq. MeOH under hydrogen atm. (1 atm) for 20 h, filtered to remove the catalyst, concd., and then similarly hydrogenated again in the presence of 14 mg 10% Pd-C for 19 h to give, after purifn. by Sephadex G-10, to give 3.3 mg I (R = H, M = Na).

IC ICM C08B037-00
ICS C07H015-10; C07H015-14; C07H015-18
ICA A61K031-725
CC 33-7 (Carbohydrates)
Section cross-reference(s): 1
ST dermatan sulfate prepn anticoagulant
IT Anticoagulants and Antithrombotics
(prepn. of dermatan sulfate as anticoagulant and intermediates for its prepn.)
IT 118711-49-2P 156977-10-5P 156977-11-6P 156977-12-7P
156977-13-8P 156977-14-9P 156977-15-0P 156977-22-9P
156977-23-0P 156977-24-1P 156977-25-2P 156977-26-3P
157085-35-3P 163214-26-4P 163214-27-5P 163214-28-6P
163214-29-7P 163214-30-0P 163214-31-1P 163214-32-2P
163214-33-3P 163214-34-4P 163214-35-5P 163214-36-6P
163214-37-7P 163214-38-8P 163214-39-9P 163214-40-2P
163214-41-3P 163214-42-4P 163214-43-5P 163214-44-6P
163214-45-7P 163214-46-8P 163214-47-9P 163214-48-0P
163214-49-1P 163214-50-4P 163214-51-5P 163214-52-6P
163214-53-7P 163214-54-8P 163214-55-9P 163214-56-0P
163214-57-1P 163214-58-2P 163214-59-3P 163214-60-6P
163214-61-7P 163214-62-8P 163214-63-9P 163214-64-0P
163214-65-1P 163214-66-2P 163214-67-3P 163214-68-4P
163214-69-5P 163214-70-8P 163214-71-9P 163214-72-0P
163214-73-1P 163214-74-2P 163214-75-3P 163379-28-0P

163379-29-1P 163379-30-4P 163379-31-5P 163379-32-6P
163379-33-7P 163379-34-8P 163379-35-9P 163379-36-0P
163379-37-1P 163379-38-2P 163379-39-3P 163512-29-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate for prepn. of dermatan sulfate as anticoagulant)

IT 138855-61-5P 156977-09-2P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dermatan sulfate as anticoagulant and intermediates for its prepn.)

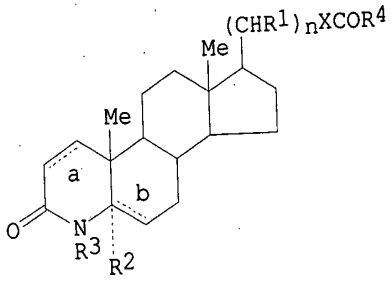
IT 100-44-7, Benzyl chloride, reactions 100-51-6, Benzenemethanol, reactions 106-95-6, Allyl bromide, reactions 107-18-6, Allyl alcohol, reactions 108-24-7, Acetic anhydride 150-76-5, p-Methoxyphenol 507-09-5, Thioacetic acid, reactions 545-06-2, Trichloroacetonitrile 874-60-2 1125-88-8, Benzaldehyde dimethyl acetal 3282-30-2, Pivaloyl chloride 17314-32-8 24355-28-0 40608-06-8, Levulinic anhydride 103703-01-1 163379-27-9
RL: RCT (Reactant)
(reaction in prepn. of dermatan sulfate as anticoagulant)

L15 ANSWER 13 OF 16 MARPAT COPYRIGHT 2002 ACS
(ALL HITs ARE ITERATION INCOMPLETES)

ACCESSION NUMBER: 121:109397 MARPAT
TITLE: Preparation of ester derivatives of 4-azasteroids as steroid 5.alpha.-reductase inhibitors.
INVENTOR(S): Witzel, Bruce E.; Rasmusson, Gary H.; Tolman, Richard L.; Yang, Shu Shu
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323041	A1	19931125	WO 1993-US4771	19930519
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9342525	A1	19931213	AU 1993-42525	19930519
AU 668181	B2	19960426		
EP 649306	A1	19950426	EP 1993-911362	19930519
EP 649306	B1	20010110		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07508039	T2	19950907	JP 1993-503838	19930519
AT 198601	E	20010115	AT 1993-911362	19930519
US 5610162	A	19970311	US 1994-338573	19941117
			US 1992-886022	19920520
PRIORITY APPLN. INFO.:			WO 1993-US4771	19930519

GI



I

AB Title compds. [I; a, b = single bonds, R2 = H; or a = single bond, b = double bond, and R2 = null; R1 = H, aryl, alkyl, aralkyl; R3 = H, Me, Et, OH, NH2, SMe; n = 0-10; X = O, S; R4 = (substituted) alkyl, aryl, heterocyclyl, cycloalkyl, amino, OH, etc.] were prepd. as inhibitors of 5.alpha.-reductase and isoenzymes thereof. The compds. are useful for the treatment of hyperandrogenic disease conditions and diseases of the skin and scalp (no data). Thus, 20-hydroxy-4-methyl-5.alpha.-4-azapregnan-3-one, 11-ethylthioundecanoic acid, DMAP, and DCC were stirred in CH2Cl2 at room temp. to give 20-[11-(ethylthio)undecanoyloxy]-4-methyl-5.alpha.-4-azapregnan-3-one.

IC ICM A61K031-435
ICS C07D221-02

CC 32-4 (Steroids)
Section cross-reference(s): 1

ST azasteroid ester prepn steroid reductase inhibitor

IT Hirsutism
(female, treatment of, azasteroid esters for)

IT Acne
(treatment of, azasteroid esters for)

IT Prostate gland
(disease, benign hyperplasia, treatment of, azasteroid esters for)

IT Prostate gland
(disease, prostatitis, treatment of, azasteroid esters for)

IT Alopecia
(male pattern, treatment of, azasteroid esters for)

IT Prostate gland
(neoplasm, carcinoma, treatment of, azasteroid esters for)

IT 9081-34-9, 5.alpha.-Steroid reductase
RL: USES (Uses)
(inhibitors, azasteroid esters as)

IT 104214-41-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 156804-81-8P 156804-82-9P 156804-83-0P 156804-84-1P
156804-85-2P 156804-86-3P 156804-87-4P 156804-88-5P
156804-89-6P 156804-90-9P 156804-91-0P 156804-92-1P
156804-93-2P 156804-94-3P 156804-95-4P 156804-96-5P
156804-97-6P 156804-98-7P 156804-99-8P 156805-00-4P
156805-01-5P 156805-02-6P 156805-03-7P 156805-04-8P
156805-05-9P 156805-06-0P 156805-07-1P 156805-08-2P
156805-09-3P 156805-10-6P 156805-11-7P 156805-12-8P
156805-13-9P 156805-14-0P 156805-15-1P 156805-16-2P
156805-17-3P 156805-18-4P 156805-19-5P 156805-20-8P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as steroid 5.alpha.-reductase inhibitor)

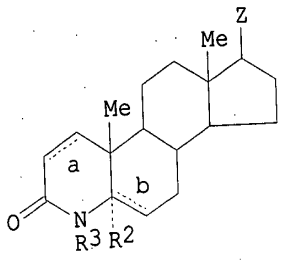
IT 624-83-9, Methyl isocyanate 627-03-2, Ethoxyacetic acid 1609-86-5, tert-Butyl isocyanate 3173-56-6, Benzyl isocyanate 3282-30-2, Trimethylacetyl chloride 38460-95-6, 10-Undecenoyl chloride 76318-67-7 86284-02-8 104319-27-9 114019-70-4, 11-Ethylthioundecanoic acid 144879-14-1 156804-93-2 156805-21-9 156924-96-8
RL: RCT (Reactant)
(reaction of, in prepn. of steroid 5.alpha.-reductase inhibitor)

L15 ANSWER 14 OF 16 MARPAT COPYRIGHT 2002 ACS
(ALL HITs ARE ITERATION INCOMPLETES)

ACCESSION NUMBER: 120:245602 MARPAT
TITLE: Preparation of 17-ethers and thioethers of 4-aza-steroids as steroid reductase inhibitors
INVENTOR(S): Witzel, Bruce E.; Tolman, Richard L.; Rasmusson, Gary H.; Bakshi, Raman K.; Yang, Shu Shu
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323040	A1	19931125	WO 1993-US4746	19930519
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9342521	A1	19931213	AU 1993-42521	19930519
AU 668180	B2	19960426		
EP 641204	A1	19950308	EP 1993-911358	19930519
EP 641204	B1	20000816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07508038	T2	19950907	JP 1993-503831	19930519
AT 195530	E	20000915	AT 1993-911358	19930519
ES 2148229	T3	20001016	ES 1993-911358	19930519
US 5536727	A	19960716	US 1994-338572	19941117
			US 1992-886031	19920520
PRIORITY APPLN. INFO.:			WO 1993-US4746	19930519

GI



I

AB Title compds. [I; a, b both = single bonds, and R2 = H; or a = double bond, b = single bond, and R2 = H; or a = single bond, b = double bond, and R2 = null; R1 = H, aryl, (aryl)alkyl; R3 = H, Me, Et, OH, NH2, SMe; R4 = (substituted) alkyl, aryl, heterocyclyl; Z = XR4, (CHR1)nXR4; X = O, S, SO, SO2], were prepd. as inhibitors of steroid 5.alpha.-reductase enzymes 1 and 2 (no data). The compds. are useful for the treatment of hyperandrogenic disease conditions and diseases of the skin and scalp. Thus, 17-hydroxymethyl-4-methyl-5.alpha.-4-azaandrostan-3-one and diphenyldiazomethane in CH2Cl2 were treated dropwise with BF3.Et2O to give 17-diphenylmethoxymethyl-4-methyl-5.alpha.-4-azaandrostan-3-one.

IC ICM A61K031-435
ICS C07D221-02

CC 32-4 (Steroids)
Section cross-reference(s): 1

ST azasteroid ether prepn reductase inhibitor; testosterone reductase inhibitor azasteroid ether; prostatitis treatment azasteroid ether; hyperplasia treatment azasteroid ether; hirsutism treatment azasteroid ether; carcinoma prostatic treatment azasteroid ether

IT Hirsutism
(female, treatment of, azasteroid ethers for)

IT Acne
(treatment of, azasteroid ethers for)

IT Steroids, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(4-aza-, 17-(thio)ethers, prepn. of, as steroid reductase inhibitors)

IT Prostate gland
(disease, benign hyperplasia, treatment of, azasteroid ethers for)

IT Prostate gland
(disease, prostatitis, treatment of, azasteroid ethers for)

IT Alopecia
(male pattern, treatment of, azasteroid ethers for)

IT Prostate gland
(neoplasm, carcinoma, treatment of, azasteroid ethers for)

IT 9081-34-9, 5.alpha.-Reductase
RL: USES (Uses)
(inhibitors, azasteroid ethers as)

IT 153946-18-0P 153946-19-1P 153946-20-4P 153946-21-5P
153946-22-6P 153946-23-7P 153946-24-8P 153946-25-9P
153946-27-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for steroid 5.alpha.-reductase inhibitor)

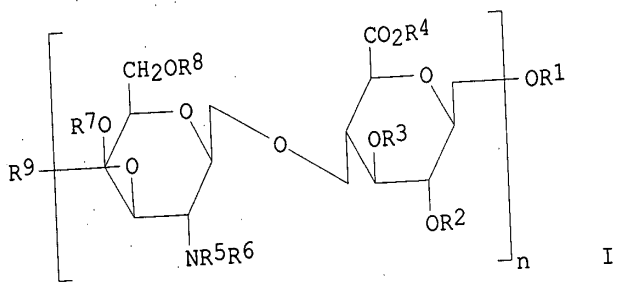
IT 153945-26-7P 153945-27-8P 153945-28-9P 153945-29-0P
153945-30-3P 153945-31-4P 153945-32-5P 153945-33-6P
153945-34-7P 153945-35-8P 153945-36-9P 153945-37-0P
153945-38-1P 153945-39-2P 153945-40-5P 153945-41-6P
153945-42-7P 153945-43-8P 153945-44-9P 153945-45-0P
153945-46-1P 153945-47-2P 153945-48-3P 153945-49-4P
153945-50-7P 153945-51-8P 153945-52-9P 153945-53-0P
153945-54-1P 153945-55-2P 153945-56-3P 153945-57-4P
153945-58-5P 153945-59-6P 153945-60-9P 153945-61-0P
153945-62-1P 153945-63-2P 153945-64-3P 153945-65-4P
153945-66-5P 153945-67-6P 153945-68-7P 153945-69-8P
153945-70-1P 153945-71-2P 153945-72-3P 153945-73-4P
153945-74-5P 153945-75-6P 153945-76-7P 153945-77-8P
153945-78-9P 153945-79-0P 153945-80-3P 153945-81-4P
153945-82-5P 153945-83-6P 153945-84-7P 153945-85-8P
153945-86-9P 153945-87-0P 153945-88-1P 153945-89-2P
153945-90-5P 153945-91-6P 153945-92-7P 153945-93-8P
153945-94-9P 153945-95-0P 153945-96-1P 153945-97-2P
153945-98-3P 153945-99-4P 153946-00-0P 153946-01-1P
153946-02-2P 153946-03-3P 153946-04-4P 153946-05-5P
153946-06-6P 153946-07-7P 153946-08-8P 153946-09-9P
153946-10-2P 153946-11-3P 153946-12-4P 153946-13-5P
153946-14-6P 153946-15-7P 153946-16-8P 153946-17-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as steroid 5.alpha.-reductase inhibitor)

IT 70-34-8, 2,4-Dinitrofluorobenzene 75-12-7, Formamide, reactions
92-69-3, 4-Hydroxybiphenyl 99-92-3, 4-Aminoacetophenone
102-49-8, 3,4-Dichlorobenzylamine 324-74-3, 4-Fluorobiphenyl
334-88-3, Diazomethane 350-46-9 352-32-9, 4-Fluorotoluene
352-33-0, 4-Fluorochlorobenzene 372-47-4, 3-Fluoropyridine
405-99-2, 4-Fluorostyrene 460-00-4, 4-Fluorobromobenzene
623-73-4, Ethyl diazoacetate 638-45-9, Hexyl iodide 769-92-6
811-51-8, Sodium thioethoxide 883-40-9, Diphenyldiazomethane
933-40-4, 1,1-Dimethoxycyclohexane 1194-02-1 4377-33-7,
2-Picolyl chloride 20607-43-6 52267-51-3, Benzyl diazoacetate
86283-92-3 86284-02-8 104214-41-7 104319-27-9 153946-26-0
153946-28-2 153946-29-3 154006-53-8
RL: RCT (Reactant)
(reaction of, in prepn. of steroid 5.alpha.-reductase inhibitor)

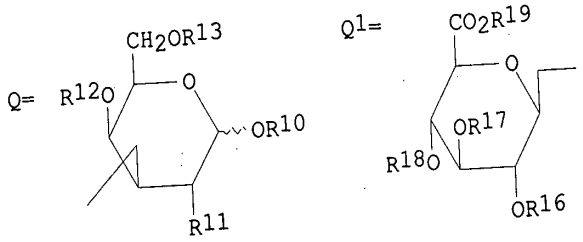
L15 ANSWER 15 OF 16 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 120:54898 MARPAT
TITLE: Preparation of galactosamine derivatives as antiinflammatory and antiallergic agents
INVENTOR(S): Oosawa, Nobuo; Takahashi, Yasuo; Kato, Kazuo; Nishijima, Kazumi
PATENT ASSIGNEE(S): Mochida Pharm Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05178876	A2	19930720	JP 1991-346911	19911227

GI



I



AB Galactosaminylglucuronic acid derivs. [I; R1 = H, protecting group, Q; R9 = H, protecting group, Q1; R11 = N3, NR14R15; R2 - R8, R10, R12, R14 - R19 = H, protecting group; n = 0-4; provided that when n = 0, R1 = Q and R9 = Q1; when n = 4, R1 and R9 = H, protecting group; the protecting group = linear or branched (un)substituted C1-8 alkyl, C2-8 alkenyl, or C1-8 acyl, (un)substituted arom. acyl, etc.], also useful as hyaluronidase inhibitors and bronchodilators, are prepd. Thus, glycosidation of 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-.alpha.-D-galactopyranosyl bromide with benzyl 2,3-di-O-benzyl-6-O-(4'-methoxybenzyl)-.alpha.-D-glucopyranoside (prepn. given) in the presence of Ag triflate, 2,4,6-collidine, and mol. sieve 4A in ClCH2CH2Cl at -25.degree. to room temp. gave benzyl 2,3-di-O-benzyl-4-O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-.beta.-D-galactopyranosyl)-6-O-(4'-methoxybenzyl)-.alpha.-D-glucopyranoside. Deprotection of the latter with NaOMe in MeOH and then with hydrazine hydrate in refluxing methanol followed by acetylation with Ac2O in pyridine and removal of 4-methoxybenzyl group with 2,3-dichloro-5,6-dicyano-p-benzoquinone in H2O-CH2Cl2 gave benzyl 2,3-di-O-benzyl-4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-.beta.-D-galactopyranosyl)-.alpha.-D-glucopyranoside. Oxidn. of the latter with CrO3 in aq. H2SO4 and acetone at -5.degree., esterification of the resulting glucuronic acid deriv. with ClCH2OMe in DMF contg. Et3N, and hydrogenolysis of the resulting glucuronic acid methoxymethyl ester over 10% Pd-C in MeOH followed by acetylation with Ac2O in pyridine, acid hydrolysis with a few drops of aq. 1M HCl in MeOH, and deacetylation with NaOMe in MeOH gave 4-O-(2-acetamido-2-deoxy-.beta.-galactopyranosyl)-D-glucuronic acid (II). II and .beta.-D-GlcA-(1.fwdarw.3)-.beta.-D-GalNAc-(1.fwdarw.4)-.beta.-D-GlcA-(1.fwdarw.3)-D-GalNAc at 1.5 mg/mL inhibited 24.0 and 60.3% hyaluronidase, resp. A capsule formulation contg. II was given. A total of 9 I were prepd.

IC ICM C07H007-033
ICS A61K031-70; C12N009-99
ICA C07H013-06; C07H015-10
CC 33-8 (Carbohydrates)
Section cross-reference(s): 1, 7, 63
ST galactosamine contg oligosaccharide prepn antiinflammatory; galactosaminylglucuronic acid prepn hyaluronidase inhibitor; antiallergic galactosaminylglucuronic acid oligosaccharide
IT Allergy inhibitors
Bronchodilators
Inflammation inhibitors
(galactosaminylglucuronic acid and its derivs. and oligosaccharides)
IT Oligosaccharides
RL: SPN (Synthetic preparation); PREP (Preparation)
(galactosaminylglucuronic acid-contg., prepn. of, as antiinflammatory and antiallergic agents and hyaluronidase inhibitors)
IT 80449-31-6, Urinastatin
RL: RCT (Reactant)
(enzymic hydrolysis of, in prepn. of galactosaminylglucuronic acid hyaluronidase inhibitor)
IT 9001-54-1, Hyaluronidase
RL: USES (Uses)
(inhibitors, galactosaminylglucuronic acid and its derivs. and oligosaccharides)
IT 2746-25-0P, p-Methoxybenzyl bromide 13435-89-7P 84872-53-7P
151722-07-5P 151722-08-6P 151722-19-9P 151722-20-2P
151722-27-9P 151722-28-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antiinflammatory and antiallergic agent and hyaluronidase inhibitor)
IT 58527-86-9P, Benzyl 2,3-di-O-benzyl-.alpha.-D-glucopyranoside
151722-09-7P 151722-10-0P 151722-11-1P 151722-12-2P
151722-13-3P 151722-14-4P 151722-15-5P 151722-16-6P
151722-17-7P 151722-18-8P 151722-21-3P 151722-22-4P
151722-23-5P 151722-24-6P 151722-25-7P 151722-26-8P
151722-29-1P 151722-30-4P 151722-31-5P 151722-32-6P
151767-04-3P 151767-05-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for galactosaminylglucuronic acid hyaluronidase inhibitor)
IT 76-83-5, Trityl chloride 105-13-5, p-Methoxybenzyl alcohol
107-30-2, Chloromethyl methyl ether 108-24-7, Acetic anhydride
334-88-3, Diazomethane 883-40-9, Diphenyldiazomethane 58527-85-8
81704-03-2 87326-36-1 87326-44-1 101973-51-7
RL: RCT (Reactant)
(reaction of, in prepn. of galactosaminylglucuronic acid hyaluronidase inhibitor)

L15 ANSWER 16 OF 16 MARPAT COPYRIGHT 2002 ACS
(ALL HITs ARE ITERATION INCOMPLETES)
ACCESSION NUMBER: 119:188311 MARPAT
TITLE: Cosmetic or dermatological composition in the form of an oil-in-water dispersion capable of forming composite films.
INVENTOR(S): Arnaud, Pascal; Mellul, Myriam
PATENT ASSIGNEE(S): Oreal S. A., Fr.

SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316684	A1	19930902	WO 1993-FR204	19930226
W: CA, JP, US RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2687932	A1	19930903	FR 1992-2296	19920227
FR 2687932	B1	19940819		
CA 2109195	AA	19930828	CA 1993-2109195	19930226
EP 583459	A1	19940223	EP 1993-905440	19930226
EP 583459	B1	19960320		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, SE				
JP 06507422	T2	19940825	JP 1993-514605	19930226
AT 135564	E	19960415	AT 1993-905440	19930226
ES 2086935	T3	19960701	ES 1993-905440	19930226
PRIORITY APPLN. INFO.:			FR 1992-2296	19920227
			WO 1993-FR204	19930226

AB The title dispersions comprise a fluorinated oil (fluorosilicone or fluorohydrocarbon) and a water-sol. polymer, such as PVA, poly(vinyl alc.-vinyl acetate) or poly(vinyl alc.-ethylene). An eye liner (pH 6.5; triethanolamine) comprised: Carbopol-941 0.20, hydroxyethylcellulose 0.30, Mowiol 18-88 1.00, Fomblin HC25 (perfluoro polyether) 5.00, glycerol 3.00, Fe oxide black pigment 10.00, and water to 100.00 g.

IC ICM A61K007-48
ICS A61K007-00; A61K007-06; A61K007-043

CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 63

ST film forming cosmetic oil water dispersion

IT Cosmetics
(film-forming, oil-in-water dispersions)

IT Cosmetics
(eye liners, oil-in-water dispersions)

IT Cosmetics
(face masks, oil-in-water dispersions)

IT Polyethers, uses
RL: BIOL (Biological study)
(fluorine-contg., cosmetics contg., film-forming, as oil-in-water dispersion)

IT Siloxanes and Silicones, compounds
RL: BIOL (Biological study)
(fluorine-contg., film-forming, as oil-in-water dispersions, for cosmetics)

IT Hydrocarbons, uses
RL: BIOL (Biological study)
(fluoro, cosmetics contg., film-forming, as oil-in-water dispersion)

IT Cosmetics
Hair preparations
(gels, oil-in-water dispersions)

IT Fluoropolymers

RL: BIOL (Biological study)
(polyether-, cosmetics contg., film-forming, as oil-in-water dispersion)

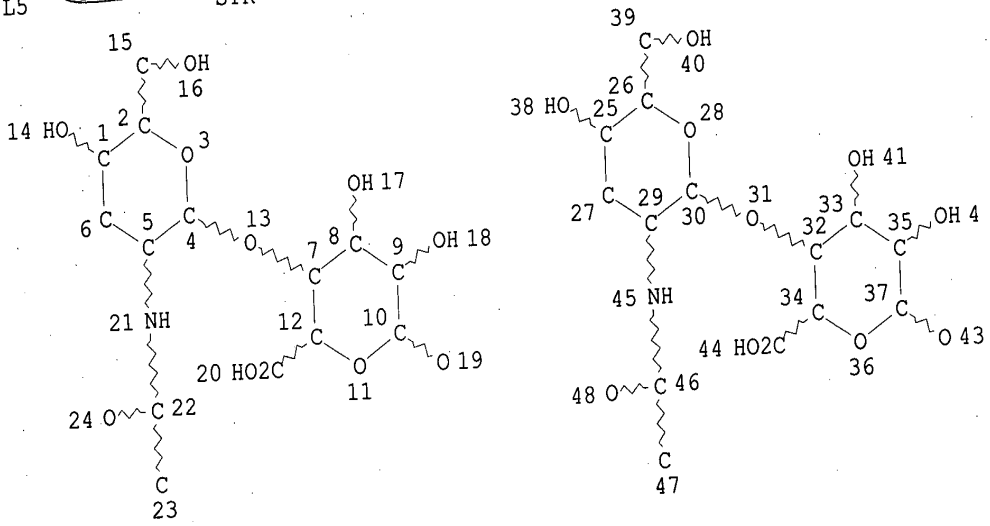
IT Fluoropolymers
RL: BIOL (Biological study)
(siloxane-, film-forming, as oil-in-water dispersions, for cosmetics)

IT Pharmaceutical dosage forms
(topical, film-forming, oil-in-water dispersions)

IT 9002-89-5, PVA 25067-34-9, Poly(vinyl alcohol-ethylene) 25213-24-5, Poly(vinyl alcohol-vinyl acetate)
RL: BIOL (Biological study)
(cosmetics contg., film-forming, as oil-in-water dispersion)

FILE 'MARPATPREV' ENTERED AT 12:05:27 ON 27 JUN 2002

L5 STR



Page 1-A

2

Page 1-B
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 48

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
MLEVEL IS CLASS ON RING NODES AND RING GROUPS
MLEVEL IS CLASS ON CHAIN NODES AND CHAIN GROUPS
ECLEVEL IS UNLIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L16 0 SEA FILE=MARPATPREV SSS FUL L5 (MODIFIED ATTRIBUTES)

-key terms

FILE 'REGISTRY' ENTERED AT 15:14:43 ON 27 JUN 2002
L1 1 S HYALURONIC ACID/CN
L5 2 S GLUCURONIC ACID/CN

FILE 'HCAPLUS' ENTERED AT 15:19:23 ON 27 JUN 2002
L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON HYALURONIC ACID/CN
L2 17048 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR HYALURONIC OR HA(S)HYALURON### OR HYALURONATE OR (GROUP(W)(A OR C))(5A)STREPTOCOCC? OR (GAS OR GCS)(S)STREPTOCOCC?
L3 3896 SEA FILE=HCAPLUS ABB=ON PLU=ON L2(20A)(CONJUGAT? OR COUPL? OR LINK? OR BOUND OR BIND?)
L4 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND ((PROTEIN OR POLYPROTEIN OR PEPTIDE OR POLYPEPTIDE)(5A)CARRIER)

L4 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:344883 HCAPLUS
DOCUMENT NUMBER: 136:345823
TITLE: Sustained-release preparations of bFGF and their manufacture
INVENTOR(S): Igarashi, Rie; Kitagawa, Akira; Mizushima, Hiroshi
PATENT ASSIGNEE(S): Ltt Inst. Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002128694	A2	20020509	JP 2000-323750	20001024

AB The prepns. are manufd. by mixing bFGF with soln. of acidic mucopolysaccharides such as Na chondroitin sulfate and Na **hyaluronate**, and human .gamma.-globulin soln., acidifying the mixt., centrifuging the mixt., removing the supernatant, suspending the insol. **conjugates** in buffer with pH 6-8 to form small particles, and optionally freeze-drying or recentrifuging the suspension. BFGF was mixed with PBS soln. of .gamma.-globulin and PBS soln. of Na chondroitin sulfate and the mixt. was acidified at 3 with HCl. The mixt. was centrifuged and supernatant was replaced with HSA-contg. PBS. The suspension was recentrifuged to give a pellet. The pellet was s.c. implanted to the back of a rat to induce neovascularization.

L4 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:112623 HCAPLUS
DOCUMENT NUMBER: 136:277743
TITLE: Lipoamino Acid-Based Adjuvant Carrier System: Enhanced Immunogenicity of **Group A Streptococcal** Peptide Epitopes
AUTHOR(S): Horvath, Aniko; Olive, Colleen; Wong, Allan; Clair, Timothy; Yarwood, Penny; Good, Michael; Toth, Istvan
CORPORATE SOURCE: School of Pharmacy, The University of Queensland, Brisbane, 4072, Australia

SOURCE: Journal of Medicinal Chemistry (2002), 45(6), 1387-1390
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lipoamino acid-based synthetic peptides (lipid core peptides, LCP) derived from the type-specific and conserved region determinants of **group A streptococci** (**GAS**) were evaluated as potential candidate sequences in a vaccine to prevent **GAS**-assocd. diseases, including rheumatic heart disease and post-**streptococcal** acute glomerulonephritis. The LCP peptides had significantly enhanced immunogenicity as compared with the monomeric peptide epitopes. Furthermore, the peptides incorporated into the LCP system generated epitope-specific antibodies without the use of any conventional adjuvant.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798086 HCAPLUS
DOCUMENT NUMBER: 135:348866
TITLE: RHAMM peptide **conjugates** for drug targeting
INVENTOR(S): Woloski, B. Michael R.; Williams, Ashley Martin; Sereda, Terrance Jimmy; Wiebe, Deanna June
PATENT ASSIGNEE(S): Cangene Corporation, Can.
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001080899	A2	20011101	WO 2001-CA533	20010420

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-198613P P 20000420
OTHER SOURCE(S): MARPAT 135:348866

AB The present invention provides protein **conjugates** having a glucose-aminoglycan-targeting domain **conjugated** directly or indirectly to a therapeutically useful protein via chem. or peptidyl **linkage**. A **conjugate** of the invention is disclosed in which a hyaluronan-**binding** protein is a receptor for **hyaluronic** acid-mediated mobility (RHAMM). The protein **conjugates** selectively target certain tissues

and organs and are useful for treating or preventing various physiol. and pathol. conditions. Methods of their use and prepn. are described.

L4 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:780644 HCAPLUS
DOCUMENT NUMBER: 135:322743
TITLE: Sustained release drug compositions containing a mucopolysaccharide
INVENTOR(S): Mizushima, Yutaka; Igarashi, Rie; Kitagawa, Aki; Takagi, Yukie
PATENT ASSIGNEE(S): Ltt Institute Co., Ltd., Japan
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078682	A2	20011025	WO 2001-JP3287	20010417
WO 2001078682	A3	20020418		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2002003398	A2	20020109	JP 2000-203850	20000705
US 2002019336	A1	20020214	US 2001-834103	20010412
PRIORITY APPLN. INFO.:			JP 2000-115091 A	20000417
			JP 2000-203850 A	20000705

AB The invention relates to a compn. providing sustained release of a drug, the compn. including (1) a mucopolysaccharide, e.g., chondroitin sulfate or **hyaluronate**, a **carrier protein**, such as .gamma.-globulin, albumin, fibrinogen, histone, etc., and a drug or (2) a mucopolysaccharide and a protein drug, such as, erythropoietin, granulocyte colony stimulating factor, thrombopoietin, antibodies, interferons, etc. For example, Na chondroitin sulfate and human .gamma.-globulin were mixed in a wt. ratio of 1:4, 1:3, 1:2, 1:1, and 2:1, resp., with the concn. of the chondroitin being fixed at 1% of compn. wt. The pH of the pptg. soln. was lowered to .apprx. pH 3, and an insol. product was obtained by centrifugation. The harvested insol. product was then suspended in a phosphate buffered saline (pH 7.2) for a release test. Compns. with ratio of 1:2 and 1:3 provided release of more drug than other ratios.

IT **9004-61-9**, **Hyaluronic** acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained release drug compns. contg. mucopolysaccharide and **carrier protein**)

L4 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:322648 HCAPLUS
DOCUMENT NUMBER: 135:185307
TITLE: Characteristics of tissue distribution of various polysaccharides as drug carriers: influences of molecular weight and anionic charge on tumor targeting
AUTHOR(S): Sugahara, Shuichi; Okuno, Satoshi; Yano, Toshiro; Hamana, Hiroshi; Inoue, Kazuhiro
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2001), 24(5), 535-543
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using the Walker 256 model for carcinosarcoma-bearing rats, we i.v. administered 5 polysaccharide carriers with various mol. wts. (MWs) and elec. charges and tested for their plasma and tissue distribution. Two carriers, carboxymethylated-D-manno-D-glucan (CMMG) and CMdextran (CMDex), showed higher plasma AUC than the other carriers tested, namely, CMchitin (CMCh), N-desulfated N-acetylated heparin (DSH), and **hyaluronic** acid (**HA**). This was consistently found to be true over the range of MWs tested. For CMDex, the max. value of plasma AUC was obtained when the MW exceeded 150 kDa. As for the anionic charge, CMDex (110-180 kDa) with a degree of substitution (DS) of the CM groups ranging from 0.2 to 0.6, showed max. plasma AUC values. Twenty-four hours after administration, the concn. of CMDex (180-250 kDa; DS: 0.6-1.2) in tumors was more than 3% of dose/g-approx. 10-fold higher than those obsd. with CMCh, DSH and HA. Doxorubicin (DXR) was **bound** to these **carriers** via a **peptide** spacer, GlyGlyPheGly (GGFG), to give **carrier**-GGFG-DXR **conjugates** (DXR content: 4.2-7.0 (wt./wt.)%), and the antitumor effects of these **conjugates** were tested with Walker 256 carcinosarcoma-bearing rats by monitoring the tumor wts. after a single i.v. injection. Compared with free DXR, CMDex-GGFG-DXR and CMMG-GGFG-DXR **conjugates** significantly suppressed tumor growth, while the CMCh-GGFG-DXR, DSH-GGFG-DXR, and HA-GGFG-DXR **conjugates** in a similar comparison showed weak tumor growth inhibition. These findings suggest that the antitumor effect of the carrier-DXR **conjugates** was related to the extent with which the carriers accumulated in the tumors.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:319762 HCAPLUS
DOCUMENT NUMBER: 134:325189
TITLE: Novel method of determining antibody response to pneumococcal capsular polysaccharide **conjugate** vaccine in humans
INVENTOR(S): Laferriere, Craig Antony Joseph; Poolman, Jan; Slaoui, Moncef Mohamed
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030390	A2	20010503	WO 2000-EP10733	20001027
WO 2001030390	A3	20020404		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-25559 A 19991028

AB The present invention relates to the field of methods of testing a vaccine response in an animal model to obtain information on the response of humans to the same vaccinogen. The present invention provides a method of detg. the dose response of a human to a polysaccharide **conjugate** vaccine comprising an immunogenic **carrier protein** and a bacterial polysaccharide, said method comprising the steps of administering to an infant animal a dose amt. of said **conjugated** vaccine, and detg. the immune response of the animal to the bacterial polysaccharide as a measure of the immune response of a human. Preferred modes of administration of vaccine in the model, dose of vaccine tested, time between doses, time of serum harvesting, method of detn. of immune response, and type (and age) of infant animal used are also all provided.

L4 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:755211 HCAPLUS
DOCUMENT NUMBER: 133:340208
TITLE: Novel compositions useful for delivering anti-inflammatory agents into a cell
INVENTOR(S): Unger, Evan C.; McCreery, Thomas; Sadewasser, David A.
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1046394	A2	20001025	EP 2000-303249	20000418
EP 1046394	A3	20011010		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-294623 A 19990419

AB The present invention is directed, inter alia, to compns. and their use for delivering compds. into a cell. In a preferred embodiment, the compns. comprise, in combination with the compd. to be delivered, an org. halide, a targeting ligand, and a nuclear localization sequence, optionally in the presence of a carrier. Ultrasound may be applied, if desired. The compns. are particularly suitable for the treatment of inflammatory diseases.

IT **9004-61-9, Hyaluronic** acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **carrier; peptide** compns. useful for delivering anti-inflammatory agents into a cell)

L4 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:553214 HCAPLUS
DOCUMENT NUMBER: 133:155448
TITLE: Pharmaceutical compositions of hydrophobically modified hedgehog proteins and their use
PATENT ASSIGNEE(S): Roche Diagnostics G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1025861	A1	20000809	EP 1999-101643	19990204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2000045848	A1	20000810	WO 2000-EP847	20000203
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1150716	A1	20011107	EP 2000-902654	20000203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 1999-101643 A 19990204
WO 2000-EP847 W 20000203

AB Hydrophobically modified hedgehog protein is **bound** in its active, folded form to a **carrier** comprising a biodegradable **protein** for delayed release after local administration. Preferred carriers are sol. or insol. collagen or gelatin, esp. in the form of a sponge and/or combined with an anionic polysaccharide such as **hyaluronic** acid; fibrin or elastin may also be used as carriers. The hedgehog **protein -carrier** complex may be used for repair of bone, cartilage, or neural defects. The complex is also suitable for systemic delivery, and does not induce immune or inflammatory reactions. Thus, a Fibracol (collagen-alginate) sponge, impregnated with a soln. of dipalmityl sonic hedgehog protein and lyophilized, slowly released .apprx.10% of its hedgehog protein content into

phosphate-buffered saline soln. at 37.degree.; the release rate was increased by adding collagenase to mimic in-vivo conditions.

IT **9004-61-9, Hyaluronic** acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carrier; pharmaceutical compns. of hydrophobically modified hedgehog proteins)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:449944 HCAPLUS
DOCUMENT NUMBER: 133:248406
TITLE: Secondary and tertiary structures in solutions of hyaluronan and related "shape module" anionic glycosaminoglycans
AUTHOR(S): Scott, John E.
CORPORATE SOURCE: Chemical Morphology, Medical School, Manchester University, Manchester, M13 9PT, UK
SOURCE: International Congress Series (2000), 1196(New Frontiers in Medical Sciences: Redefining Hyaluronan), 11-19
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 20 refs. **Hyaluronan** (**HA**) is chem. the simplest of a group of biopolymers, the anionic glycosaminoglycans (AGAGs), which includes the chondroitins (Ch) and keratans (Ke). They are chains of pyranose sugar units, joined via glycosidic **links** identically positioned and oriented between these units, in which only the robust C1 chair form is present. In contrast to this rigid uniformity, the interresidue **links** offer great potential flexibility. However, steric hindrance drastically restricts this variety and an array of interunit H-bonds and water bridges further decreases the possibilities to a very small no. of chain conformations of which the 2-fold helix is preferred, as shown by NMR studies. This latter structure is tape-like; both sides being identical but antiparallel, with extensive hydrophobic patches regularly placed along each side. Both sides look exactly the same, giving rise to the term "amibidexteran"; able to use both hands equally well. The polymer backbones of HA, the Chs and Kes, form almost identical 2-fold-helical ambidexterans with similarly placed hydrophobic patches. Electron microscopy of rotary-shadowed HA prepns. proved that ordered tertiary structures 'in the form of honeycomb meshworks' form spontaneously even in very dil. solns. Mol. modeling, based on the secondary structures detd. by NMR, suggested that hydrophobic and H-bonding interactions, in opposition to electrostatic repulsion, drove this self-aggregation. The shapes of the 2-fold helixes, which incorporate gentle curves in two planes at right angles, complement each other perfectly only when the interacting faces of the 2-fold helixes are antiparallel. In this orientation hydrophobic patches on adjacent ambidexterans can interact, and H-bonds between acetamido NH and carboxylates are possible. Computational anal. and electron microscopy, inter alia, showed that chondroitin-6-sulfate and keratan sulfate self-aggregate and mol. models, as well as bead aggregation assays, showed that

heteroaggregation (between unlike AGAGs, e.g., Ke and Ch) was possible. 13C-NMR studies on HA gave direct evidence that the above models were valid, and suggested the presence of a .beta.-sheet soln. structure of HA analogous to that found in proteins. Electron histochem. on tissues demonstrated that collagen fibrils are tied and bridged by AGAG filaments at regular intervals along the fibrils. Specific **binding** sites for the AGAG **carriers**, the proteoglycan **proteins**, were located and amino acid sequences proposed for these sites on the collagen fibril in the gap zone. By tailoring the length of the AGAG chain, the sepn. between collagen fibrils is defined, contributing in a major way to defining the shape of the tissue. These regular, specific, quaternary collagen-proteoglycan structures were, therefore, termed "shape modules". Possibly, HA was the first AGAG in evolution to be part of organized intercellular structures as a kind of primitive ECM (e.g., in the streptococci) and the more complicated and diverse roles of the sulfated AGAGs developed from this beginning.

IT **9004-61-9**, Hyaluronan
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(secondary and tertiary structures in solns. of hyaluronan and related "shape module" anionic glycosaminoglycans)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:314721 HCAPLUS
DOCUMENT NUMBER: 132:333381
TITLE: GRAB protein derived from Streptococcus pyogenes
INVENTOR(S): Bjorck, Lars Henrik; Rasmussen, Magnus
PATENT ASSIGNEE(S): Actinova Limited, UK
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026240	A2	20000511	WO 1999-GB3631	19991102
WO 2000026240	A3	20011011		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1144442	A2	20011017	EP 1999-954134	19991102
EP 1144442	A3	20020206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002061306	A1	20020523	US 2001-847539	20010501

PRIORITY APPLN. INFO.: GB 1998-23975 A 19981102
WO 1999-GB3631 W 19991102

AB Described is a S. pyogenes-derived protein capable of **binding** to .alpha.2 macroglobulin. The protein is termed protein GRAB, is encoded in grab gene, and comprises the amino acid sequence of SEQ ID No: 1. The invention also relates to a peptide comprising a fragment of the protein of at least six amino acids in length. A protein or peptide which is capable of generating a protective immune response to **Group A streptococcus** comprises the amino acid sequence of SEQ ID No: 1, a functional variant thereof or a functional variant of at least six amino acids in length of either thereof. Such a protein or peptide may be used in a vaccine compn. together with a pharmaceutically acceptable carrier for immunotherapy.

L4 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:241505 HCAPLUS
DOCUMENT NUMBER: 132:290233
TITLE: Sequences of peptides derived from staphylococcal and streptococcal toxins, and applications thereof in diagnosing and treating toxic shock syndrome and septic shock
INVENTOR(S): Bannan, Jason D.; Visvanathan, Kumar; Zabriskie, John B.
PATENT ASSIGNEE(S): Rockefeller University, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020598	A1	20000413	WO 1999-US22180	19990924
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960597	A1	20000426	AU 1999-60597	19990924
EP 1127132	A1	20010829	EP 1999-970123	19990924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-168303 A 19981007
US 1999-335581 A 19990618
WO 1999-US22180 W 19990924

OTHER SOURCE(S): MARPAT 132:290233

AB This invention relates to amino acid sequences of peptides useful for providing protection against, or reducing the severity of, toxic shock and septic shock resulting from bacterial infections. More particularly, the invention provides peptides derived from consensus sequences of the family of staphylococcal and streptococcal toxins, and may be polymeric and/or carrier-**conjugates** thereof.

The invention also relates to serum antibodies induced by the **peptides** and/or **carrier-conjugates** and their use to prevent, treat, or protect against the toxic effects of most, if not all, of the staphylococcal and streptococcal toxins. Antibodies may be induced by administration of a pharmaceutical compn. and/or vaccine contg. a peptide of the invention. The invention also relates to diagnostic assays and kits to detect the presence of staphylococcal and streptococcal toxins, or antibodies thereto.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:195928 HCAPLUS
DOCUMENT NUMBER: 132:212511
TITLE: Cosmetic compositions containing **hyaluronic** acid and proteins
INVENTOR(S): McKenzie, Elma
PATENT ASSIGNEE(S): S. Afr.
SOURCE: S. African, 17 pp.
CODEN: SFXXAB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 9800404	A	19981001	ZA 1998-404	19980119

AB A cosmetic skin treatment compn. comprising: from 0.1% to 75% of at least one cell therapeutic compd., substance or compn. selected from the group consisting of **hyaluronic** acid or a pharmaceutically acceptable salt thereof, a keratin **binding** complex, glycosaminoglycans, a compn. including water and glycoprotein, an uncontrolled target-oriented carrier, a hydrophilic skin moisturizing factor, a collagen amino acid, a compn. including sericin and glycoprotein, and a compn. including water, locust bean gum and hydrolyzed milk **protein**; and a cosmetically acceptable **carrier**. Formulation of a cosmetic compn. contg. 5% **hyaluronic** acid is disclosed.

IT **9004-61-9, Hyaluronic** acid
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cosmetic compns. contg. **hyaluronic** acid and proteins)

L4 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:161161 HCAPLUS
DOCUMENT NUMBER: 132:212700
TITLE: Low-molecular fragments of **hyaluronic** acid for the preparation of vaccines
INVENTOR(S): Simon, Jan; Martin, Stefan; Termeer, Christian
PATENT ASSIGNEE(S): Universitaetsklinikum Freiburg, Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012122	A2	20000309	WO 1999-EP6280	19990826
WO 2000012122	A3	20000622		

W: AU, CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

DE 19839113	A1	20000302	DE 1998-19839113	19980827
DE 19853066	A1	20000525	DE 1998-19853066	19981117
AU 9957416	A1	20000321	AU 1999-57416	19990826

PRIORITY APPLN. INFO.:
DE 1998-19839113 A 19980827
DE 1998-19853066 A 19981117
WO 1999-EP6280 W 19990826

AB Low-mol.-wt. **hyaluronic** acid (**HA**) fragments, which may be suitably modified, may be used for the prepn. of vaccines for treatment of cancer. These HA fragments can be used to produce mature dendritic cells, or alternatively, together with antigens, **peptides**, or **carrier** systems, they can be used directly as adjuvants in vaccines. The HA fragments can also be **coupled** to an antigen, **peptide**, or **carrier** system and this **coupled** system can be used as a vaccine for treatment of cancer. Thus, HA was fragmented by sonication and incubation with hyaluronidase type I. The fragments were used to stimulate dendritic cells produced from bone marrow CD14-pos. monocytes by maturation with GM-CSF and IL-4. The stimulated dendritic cells induced proliferation of naive allogenic T-cells and showed increased expression of ICAM-1, HLA-DR, B7-1, AND B7-2.

IT **9004-61-9DP, Hyaluronic** acid, fragments
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(low-mol. fragments of **hyaluronic** acid for prepn. of vaccines)

L4 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:144761 HCAPLUS
DOCUMENT NUMBER: 132:193251
TITLE: Immunogenic .beta.-propionamido-**linked** polysaccharide protein **conjugate** useful as a vaccine produced using an N-acryloylated polysaccharide
INVENTOR(S): Michon, Francis; Huang, Chun-Hsien; Uitz, Catherine
PATENT ASSIGNEE(S): North American Vaccine, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010599	A2	20000302	WO 1999-US18982	19990818

WO 2000010599 A3 20000622
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9957800 A1 20000314 AU 1999-57800 19990818
EP 1109576 A2 20010627 EP 1999-945115 19990818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI
NO 2001000805 A 20010403 NO 2001-805 20010216
PRIORITY APPLN. INFO.: US 1998-97120P P 19980819
US 1999-376911 A 19990818
WO 1999-US18982 W 19990818

AB Novel immunogenic .beta.-propionamido-**linked** polysaccharide- and N-propionamido-**linked** oligosaccharide-protein **conjugates** are provided as well as method of producing the **conjugates**. The **conjugation** procedure is simple, rapid, reproducible and applicable to a variety of polysaccharides or oligosaccharides derived from bacterial species, yeast, cancer cells or chem. synthesized. Vaccines and methods of immunization against infection or cancer using the immunogenic .beta.-propionamido-**linked** polysaccharide- and .beta.-propionamido-**linked** oligosaccharide-protein **conjugates** are also disclosed.

L4 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:640503 HCAPLUS
DOCUMENT NUMBER: 131:262638
TITLE: Pharmaceutical composition of hedgehog proteins and use thereof
INVENTOR(S): Lang, Kurt; Papadimitriou, Apollon
PATENT ASSIGNEE(S): Roche Diagnostics GmbH, Germany
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 947201	A1	19991006	EP 1999-101642	19990204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 9900471	A	19990805	NO 1999-471	19990201
BR 9900523	A	20000502	BR 1999-523	19990203
ZA 9900887	A	19990804	ZA 1999-887	19990204
AU 9915426	A1	19990826	AU 1999-15426	19990204
AU 713568	B2	19991202		
CN 1228994	A	19990922	CN 1999-101764	19990204
JP 2000119193	A2	20000425	JP 1999-27836	19990204
JP 3092706	B2	20000925		
PRIORITY APPLN. INFO.:			EP 1998-101893 A	19980204

EP 1998-104416 A 19980312

AB A pharmaceutical compn. of a hedgehog (HH) protein which is characterized in that the hedgehog **protein** is **bound** to a hydrophilic **carrier** that is biocompatible and biodegradable wherein the carrier is a polymer which **binds** the hedgehog **protein** as a neg.-charged **carrier** as a result of ionic interactions, does not denature the hedgehog **protein** when it **binds** to the **carrier**, contains at least 0.1 to 2 neg.-charged residues per monomer under neutral conditions, contains the charge in the form of acidic groups, has an av. mol. wt. of at least 50,000 Da and contains no agarose reversibly and actively releases hedgehog **proteins** in vivo from a **carrier** in a delayed manner. An alginate gel contg. HH protein was prepd. contg. sucrose, K phosphate, Na alginate and HH protein soln.

IT **9004-61-9, Hyaluronic** acid
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compn. of hedgehog proteins)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:597423 HCAPLUS
DOCUMENT NUMBER: 131:213104
TITLE: Antigenic **conjugates** of conserved lipopolysaccharides of gram negative bacteria
INVENTOR(S): Arumugham, Rasappa G.; Fortuna-Nevin, Maria; Apicella, Michael A.; Gibson, Bradford W.
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 941738	A1	19990915	EP 1999-301747	19990309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9919540	A1	19990923	AU 1999-19540	19990309
JP 11322793	A2	19991124	JP 1999-61354	19990309
BR 9902008	A	20000509	BR 1999-2008	19990309
PRIORITY APPLN. INFO.:			US 1998-37529 A	19980310

AB Antigenic **conjugates** are provided which comprise a **carrier protein** covalently bonded to the conserved portion of a lipopolysaccharide of a gram neg. bacteria, wherein said conserved portion of the lipopolysaccharide comprises the inner core and lipid A portions of said lipopolysaccharide, said **conjugate** eliciting a cross reactive immune response against heterologous strains of said gram neg. bacteria. The **carrier protein** is selected from CRM197, tetanus toxin, diphtheria toxin, pseudomonas exotoxin A, cholera toxin, **group A streptococcal** toxin, pneumolysin of **Streptococcus** pneumoniae, filamentous hemagglutinin

(FHA), FHA of Bordetella pertussis, pili or pilins of Neisseria gonorrhoeae or meningitidis, outer membrane proteins of Neisseria meningitidis, C5A peptidase of Streptococcus and surface protein of Moraxella catarrhalis.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:466154 HCAPLUS
DOCUMENT NUMBER: 131:227366
TITLE: A new vaccine concept: polysaccharide **conjugate** vaccines
AUTHOR(S): Moreau, M.
CORPORATE SOURCE: Lab. Pasteur Merieux Connaught, Marcy l'Etoile, F-69280, Fr.
SOURCE: Annales Pharmaceutiques Francaises (1999), 57(3), 223-231
CODEN: APFRAD; ISSN: 0003-4509
PUBLISHER: Masson Editeur
DOCUMENT TYPE: Journal
LANGUAGE: French

AB Polysaccharide-based vaccines such as the vaccines against Neisseiria meningitidis **group A** and C or **Streptococcus** pneumoniae have proved their efficacy in children and adults. Nevertheless they induce B cell mediated immunol. response and therefore fail to protect infants. In the eighties appeared a new concept of Polysaccharide based vaccine for infants: Polysaccharide **conjugate** vaccines. **Coupling** polysaccharide to **carrier protein** transforms the T-independent antigen into T-dependent antigen. The first **conjugate** vaccines for the prevention of infections caused by Haemophilus influenzae type b were a success, with a 95% efficacy. A worldwide vaccination program might lead to the eradication of that bacterial disease. New vaccines are currently under development, the next **conjugate** vaccine should be one against Streptococcus pneumoniae. First published clin. data are very promising and confirmed the potential of the polysaccharide **conjugate** vaccine approach against bacterial infections.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:350607 HCAPLUS
DOCUMENT NUMBER: 131:14825
TITLE: A method of increasing nucleic acid synthesis with ultrasound
INVENTOR(S): Unger, Evan C.; McCreery, Thomas; Sadewasser, David
PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925385	A1	19990527	WO 1998-US23843	19981111
W: AU, CA, JP RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9913906	A1	19990607	AU 1999-13906	19981111
PRIORITY APPLN. INFO.:			US 1997-971540	19971117
			WO 1998-US23843	19981111

OTHER SOURCE(S): MARPAT 131:14825

AB The present invention is directed to a method of increasing nucleic acid synthesis in a cell comprising administering to the cell a therapeutically effective amt. of ultrasound for a therapeutically effective time such that said administration of said ultrasound results in said increased nucleic acid synthesis. The nucleic acid sequence may comprise an endogenous sequence or an exogenous sequence. In particular, the invention is directed to increasing the expression of stress proteins and repair proteins.

IT **9004-61-9, Hyaluronic** acid **9004-61-9D,**
Hyaluronic acid, deriv.
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(carrier; method of increasing nucleic acid synthesis with ultrasound)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:56434 HCAPLUS
DOCUMENT NUMBER: 130:179625
TITLE: Measuring method for protein or ligand.
INVENTOR(S): Takei, Yoshiyuki; Honma, Tamotsu; Ito, Akio
PATENT ASSIGNEE(S): Mitsubishi Chemical Industries Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11014628	A2	19990122	JP 1997-166833	19970624

AB A simple and sensitive method is described for detecting protein or ligand. The method comprises reacting ligand or protein in the sample with **protein** or ligand fixed on **carrier** particles and detecting the change in light absorbance or scattering of the reaction mixt. upon light irradn. using the principle of latex agglutination method. A successful example is shown with **hyaluronic** acid detection using **hyaluronic** acid **binding** protein fixed on latex particles.

IT **9004-61-9, Hyaluronic** acid
RL: ANT (Analyte); ANST (Analytical study)
(measuring method for protein or ligand)

L4 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:800024 HCAPLUS
DOCUMENT NUMBER: 130:51336
TITLE: Laft mutants of pathogenic gram-negative bacteria
INVENTOR(S): Apicella, Michael A.; Gibson, Bradford W.; Nichols, Wade A.
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA; University of California
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9853851	A1	19981203	WO 1998-US10881	19980528
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877010	A1	19981230	AU 1998-77010	19980528
PRIORITY APPLN. INFO.:			US 1997-47791P P	19970528
			WO 1998-US10881 W	19980528

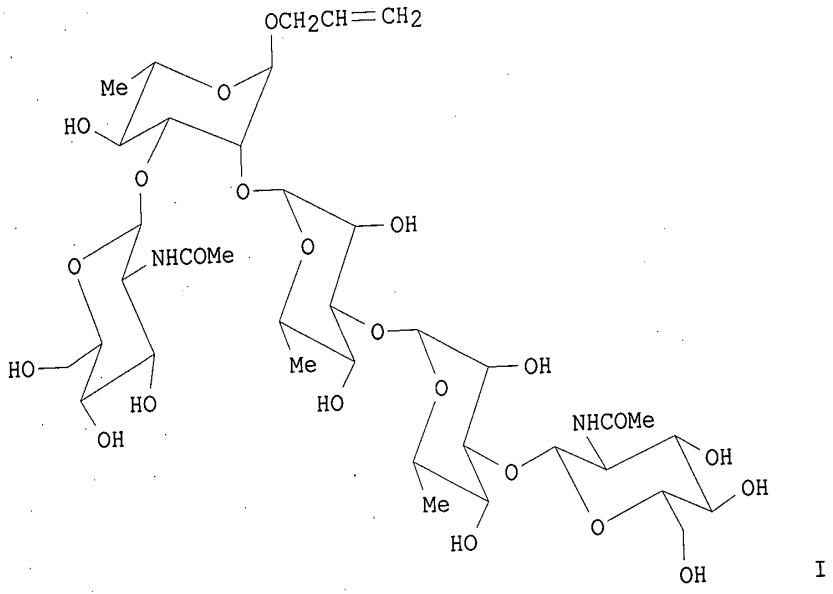
AB A method is provided for identifying, isolating, and producing lipooligosaccharide (LOS) mutants of gram-neg. bacterial pathogens. The method comprises mutating the laft gene of a gram-neg. bacterial pathogen so that there is a lack of a functional Lipid A fatty acid transferase protein. The resulting LOS mutants lack one or more secondary acyl chains as compared to the LOS contained in the wild type gram-neg. bacterial pathogen. The LOS isolated from the laft mutants displays substantially reduced toxicity as compared to that of the wild type strain. Also, the present invention provides methods for using a vaccine formulation contg. the laft mutants, the endotoxin isolated therefrom, or the endotoxin isolated therefrom which is then **conjugated** to a **carrier protein**, to immunize an individual against infections caused by gram-neg. bacterial pathogens by administering a prophylactically effective amt. of the vaccine formulation.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:611531 HCAPLUS
DOCUMENT NUMBER: 126:8398
TITLE: Efficient, convergent syntheses of oligosaccharide allyl glycosides corresponding to the **Streptococcus Group A** cell-wall polysaccharide
AUTHOR(S): Auzanneau, France-Isabelle; Forooghian, Farzxin; Pinto, B. Mario

CORPORATE SOURCE: Department Chemistry, Simon Fraser University, Brunaby, BC, V5A 1S6, Can.

SOURCE: Carbohydrate Research (1996), 291, 21-41
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Convergent syntheses of di-, tri, tetra-, penta-, and hexasaccharide allyl glycosides corresponding to the .beta.-hemolytic **Streptococcus Group A** cell-wall polysaccharide are described. The strategy relies on the prepn. of related di- and trisaccharide building blocks: .beta.-D-GlcpNAc-(1-3)-.alpha.-L-Rha-p and .alpha.-L-Rha-p-(1-2)-[.beta.-D-GlcpNAc-(1-3)]-.alpha.-L-Rha-p, which could be used either as glycosyl donors or acceptors in subsequent glycosylation reactions. The protecting groups were chosen to allow the selective removal of the allyl aglycon to access the intermediate glycosyl donors but also to allow their own removal without affecting the allyl group. The allyl group was intended for use in **conjugation** of the oligosaccharides to sol. **protein carriers** or solid supports for the prepn. of antigens and immunoadsorbents, resp. (no data). One of the target compds. was I.

L4 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:465547 HCAPLUS
DOCUMENT NUMBER: 121:65547
TITLE: Antigen of hybrid m **protein** and **carrier** for **group a streptococcal** vaccine
INVENTOR(S): Dale, James B.

PATENT ASSIGNEE(S): Univesity of Tennessee Research Corp., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9406465	A1	19940331	WO 1993-US8704	19930915
W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 618813	A1	19941012	EP 1993-922202	19930915
EP 618813	B1	20020109		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 211654	E	20020115	AT 1993-922202	19930915

PRIORITY APPLN. INFO.: US 1992-945860 A 19920916
WO 1993-US8704 W 19930915

AB Streptococcal M protein peptides that elicit protective antibodies against **Group A streptococci** and prevent rheumatic fever are manufd. as fusion proteins of N- and C-terminal peptides of the protein by expression of the gene in a microbial host. The peptides used may be shorter than those normally required for vaccines. Peptides from other **proteins** may be used as the **carrier** with the domains **linked** by a hydrophobic peptide. The protein may be administered by conventional methods, or by use of a non-pathogenic Streptococcus, e.g. a non-cariogenic S. mutans, expressing the gene. Fusion products of the M24 protein and the B subunit of Escherichia coli heat-labile enterotoxin were manufd. by expression of the gene in Escherichia coli. The proteins were purified, emulsified with complete Freund's adjuvant and 300 .mu.g of protein injected s.c. into rabbits with a booster given four weeks later. Specific opsonic antibodies against type 24 Streptococcus were obtained; these antibodies were not effective against type 5 Streptococcus. In passive mouse protection tests, the i.p. LD50 for type 24 Streptococcus was 1.5.times.105 CFU for control animals and 2.5.times.106 for animals pretreated with rabbit antiserum.

L4 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:415587 HCAPLUS
DOCUMENT NUMBER: 115:15587
TITLE: Pharmaceutical preparation containing hormones or growth factors and receptors or **binding** proteins

INVENTOR(S): Prisell, Per; Norstedt, Gunnar
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9005522	A1	19900531	WO 1989-SE666	19891117
W: AU, BB, BG, BR, DK, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, ES, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 8945253	A1	19900612	AU 1989-45253	19891117
AU 632074	B2	19921217		
EP 444081	A1	19910904	EP 1989-912690	19891117
EP 444081	B1	19990512		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05505169	T2	19930805	JP 1989-511728	19891117
JP 2752209	B2	19980518		
AT 179887	E	19990515	AT 1989-912690	19891117
ES 2134187	T3	19991001	ES 1989-912690	19891117
PRIORITY APPLN. INFO.:			SE 1988-4164	19881117
			WO 1989-SE666	19891117

AB A receptor or **binding** protein for a hormone or growth factor is **coupled** with **hyaluronic** acid gel or other biodegradable polymer carrier for use as a pharmaceutical to treat excessive prodn. of the hormone or growth factor. Addnl., a combination of the growth factor or hormone, the receptor or **binding protein**, and the **carrier** is used as a slow-release form of the growth factor or hormone. Thus, the extracellular domain of the growth hormone (GH) receptor, produced by recombinant DNA methodol., was purified, crosslinked to **hyaluronic** acid, and incubated with excess GH, and unbound GH was removed by centrifugation. This prepn., injected s.c., slowly released GH in a dose-dependent manner which was based on both the amt. of GH and the no. of GH receptors **coupled** to the gel. Hypophysectomized rats treated with this prepn. showed an increase in body wt.

IT **9004-61-9, Hyaluronic** acid
RL: BIOL (Biological study)
(pharmaceutical gel contg. growth factor/hormone and receptor/**binding** protein and)

L4 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1986:459153 HCAPLUS
DOCUMENT NUMBER:	105:59153
TITLE:	Opsonic antibodies evoked by hybrid peptide copies of types 5 and 24 streptococcal M proteins synthesized in tandem
AUTHOR(S):	Beachey, Edwin H.; Gras-Masse, Helene; Tarter, Andre; Jolivet, Michel; Audibert, Francoise; Chedid, Louis; Seyer, Jerome M.
CORPORATE SOURCE:	Veterans Adm. Med. Cent., Memphis, TN, 38104, USA
SOURCE:	J. Exp. Med. (1986), 163(6), 1451-8 CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The protective immunogenicity of a hybrid peptide contg. tandem copies of types 5 and 24 epitopes of streptococcal M protein was investigated. C-terminal peptides of the CNBr-derived fragment 7 (CB7) of type 24 M protein were chem. synthesized, and then extended to include the first 20 residues of the N-terminus of type 5M

protein. When emulsified in complete Freunds adjuvant and injected into rabbits without **conjugation** to a **carrier**, each of the synthetic hybrid **peptides**, designated S-M5(1-20)-S-CB7(23-35)C and S-M5(1-20)-S-CB(19-34), evoked opsonic antibodies against both types 5 and 24 streptococci without raising heart tissue-crossreactive immunity. These results suggest that tandem hybrid peptides may provide a new approach to the development of multivalent vaccines, not only to different serotypes of **group A streptococci** but perhaps also to a variety of other infectious agents.

L4 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:625653 HCAPLUS
DOCUMENT NUMBER: 95:225653
TITLE: **Conjugate** of streptococcal M protein peptide vaccine
INVENTOR(S): Beachey, Edwin H.
PATENT ASSIGNEE(S): United States Dept. of Health, Education, and Welfare, USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4284537	A	19810818	US 1980-165619	19800703

AB Peptide fragments of streptococcal M protein, CB6 [79585-35-6] and CB7 [79585-34-5] are **linked** covalently to a **protein carrier**, poly(lysine). This **conjugate** is immunogenic in rabbits producing protective antibodies against the whole **group A streptococci**. The complete amino acid sequence of the 2 CNBr peptide fragments CB6 and CB7 of type 24 streptococcal M protein purified from a peptic ext. of the organism was detd. by Edman degrdn. of the uncleaved peptides and their tryptic peptides. The sequence of CB6 was Asn-Phe-Ser-Thr-Ala-Asp-Ser-Ala-Lys-Ile-Lys-Thr-Leu-Gln-Ala-Glu-Lys-Ala-Ala-Leu-Glu-Ala-Arg-Gln-Ala-Glu-Leu-Glu-Lys-Ala-Leu-Gln-Gly-Ala-Hse. The sequence of CB7 was identical except for substitutions of Ala, Lys and Asp at positions 21, 24, and 26, resp. CB6 and CB7 (75 nmol) were **conjugated** with poly(lysine) (15 nmol) with carbodiimide by mixing in 1.57 mL of distd. H2O. The mixts. were stirred for 18 h at 22.degree., dialyzed for 24 h and stored at -70.degree.. Antibodies raised in rabbits against the CB6 or CB7 **conjugates** were opsonic, bactericidal and protective.

L4 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:512475 HCAPLUS
DOCUMENT NUMBER: 95:112475
TITLE: Identification of core protein, an intermediate in proteoglycan biosynthesis in cultured chondrocytes from the Swarm rat chondrosarcoma
AUTHOR(S): Kimura, James H.; Thonar, Eugene J. M.; Hascall, Vincent C.; Reiner, Agnes; Poole, A. Robin
CORPORATE SOURCE: Lab. Biochem., Natl. Inst. Dent. Res., Bethesda,

MD, 20205, USA
SOURCE: J. Biol. Chem. (1981), 256(15), 7890-7
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB After incubating cultured chondrocytes from the Swarm rat chondrosarcoma for 30 min with [3H]serine, a labeled macromol. was found predominantly as a .apprx.370,000-mol.-wt. species which was subsequently identified as a core protein precursor to cartilage proteoglycan. It was immunopptd. along with completed proteoglycan from cell exts. by an antiserum to the complex of **hyaluronic** acid-**binding** region, **link** protein, and **hyaluronic** acid. Its immunopptn. could be inhibited completely by the addn. of purified **hyaluronic** acid-**binding** region of the exts., indicating the presence of common antigenic determinants with this region of the proteoglycan core protein. The core protein precursor was able to interact with the **hyaluronic** acid and **link protein** in proteoglycan aggregates added as **carrier** to exts. to form mixed aggregates of high buoyant d. in associative CsCl d. gradients. Labeled core protein precursor and **link** protein were subsequently isolated from the mixed aggregates from the top of dissociative CsCl d. gradients. Radioactivity in core protein precursor after a 30-min pulse of [3H]serine disappeared after inhibiting further protein synthesis with cycloheximide concurrent with the appearance of label in completed proteoglycan mols.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, TOXCENTER, PHIC, PHIN' ENTERED AT 15:21:35 ON 27 JUN 2002)

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON HYALURONIC ACID/CN
L2 17048 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR HYALURONIC OR HA(S)HYALURON### OR HYALURONATE OR (GROUP(W)(A OR C))(5A)STREPTOCOCC? OR (GAS OR GCS)(S)STREPTOCOCC?
L5 2 SEA FILE=REGISTRY ABB=ON PLU=ON GLUCURONIC ACID/CN
L7 8896 SEA L2(S)(CONJUGAT? OR COUPL? OR LINK? OR BOUND OR BIND?)
L8 340 SEA L7 AND ((PROTEIN OR POLYPROTEIN OR PEPTIDE OR POLYPEPTIDE)(5A) CARRIER)
L9 8 SEA L8 AND (L5 OR GLUCURONIC OR (GLCA OR GLC)(S) GLUCURONIC)

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON HYALURONIC ACID/CN
L2 17048 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR HYALURONIC OR HA(S)HYALURON### OR HYALURONATE OR (GROUP(W)(A OR C))(5A)STREPTOCOCC? OR (GAS OR GCS)(S)STREPTOCOCC?
L7 8896 SEA L2(S)(CONJUGAT? OR COUPL? OR LINK? OR BOUND OR BIND?)
L8 340 SEA L7 AND ((PROTEIN OR POLYPROTEIN OR PEPTIDE OR POLYPEPTIDE)(5A) CARRIER)
L12 9 SEA L8 AND COVALEN?

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON HYALURONIC ACID/CN
L2 17048 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR HYALURONIC OR HA(S)HYALURON### OR HYALURONATE OR (GROUP(W)(A OR C))(5A)STREPTOCOCC? OR (GAS OR GCS)(S)STREPTOCOCC?

L7 8896 SEA L2(S)(CONJUGAT? OR COUPL? OR LINK? OR BOUND OR BIND?)

L8 340 SEA L7 AND ((PROTEIN OR POLYPROTEIN OR PEPTIDE OR POLYPEPTIDE)(5A) CARRIER)

L10 58 SEA L8 AND (LMW OR (MOL OR MOLECULAR)(W)(WT OR WEIGH?) OR MW)

L13 29 SEA L10 AND (KD? OR KILOD? OR KILO(W) DAL? OR DAL# OR DALTON OR 400KD? OR 400KILOD? OR 600DA?)

L14 43 S L9 OR L12 OR L13

L15 40 DUP REM L14 (3 DUPLICATES REMOVED)

L15 ANSWER 1 OF 40 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-308366 [32] WPIDS

DOC. NO. CPI: C2001-095258

TITLE: Sustained release microspheres for administrating drugs, comprises a **carrier protein**, a water soluble polymer, a polyanionic polysaccharide and divalent calcium or magnesium.

DERWENT CLASS: A96 B04

INVENTOR(S): BLIZZARD, C D; BROWN, L R; RASHBA-STEP, J; RISKE, F J; SCOTT, T L

PATENT ASSIGNEE(S): (EPIC-N) EPIC THERAPEUTICS INC

COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001028524	A1	20010426	(200132)*	EN	71

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001011980 A 20010430 (200148)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001028524	A1	WO 2000-US28200	20001012
AU 2001011980	A	AU 2001-11980	20001012

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001011980	A	Based on	WO 200128524

PRIORITY APPLN. INFO: US 1999-420361 19991018

AN 2001-308366 [32] WPIDS

AB WO 200128524 A UPAB: 20010611

NOVELTY - Sustained release microspheres comprising a **carrier protein** (I), a water soluble polymer (II), a first complexing agent (III) that is a polyanionic polysaccharide,

and a second complexing agent (IV) comprising a divalent metal cation comprising calcium or magnesium, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a syringe containing a single dose of the microspheres, including a needle having a bore size of 14-30 gauge; and

(2) forming a microsphere comprising:

(a) forming an aqueous mixture of (I), (II), (III) and (IV);

(b) allowing the microspheres to form in the aqueous mixture; and

(c) stabilizing the microspheres, preferably by contacting the microspheres with a crosslinking agent and/or exposing the microspheres to an energy source, preferably heat.

USE - The microspheres are useful for administration of drugs, for a wide variety of separations, diagnostic, therapeutic, industrial, commercial and research purposes e.g. in vivo diagnosis (e.g. where the microspheres can include a macromolecule such as an immunoglobulins or cell receptor labeled with a detectable label). They can be labeled for diagnosis of proliferative disorders such as cancer, or can be used for purification of molecules from complex mixtures, as reagents for detection or quantification of specific molecules or for production of molecules such as antibodies. They can also be used as adjuvants for vaccine production by injection into e.g. mice or rabbits to trigger enhanced immune responses. The microspheres can also be used in cleaning formulations such as enzyme particles for addition to detergents, cosmetics such as the formation of collagen particles to be suspended in a lotion or cream, ink or paint.

ADVANTAGE - Prior art micro particles or beads were difficult and expensive to produce and had a wide size distribution, often lacked uniformity and failed to exhibit long term release kinetics when the concentration of active ingredients was high. The new microspheres are of a dimension which permits the delivery using a needleless syringe, eliminating disposal problems inherent to needles which must be disposed as biohazard waste products. The microspheres also have qualities suitable for delivery by other parenteral and non-parenteral routes.

Dwg.0/13

DUPLICATE 1

L15 ANSWER 2 OF 40 MEDLINE

ACCESSION NUMBER: 2001294683 MEDLINE

DOCUMENT NUMBER: 21270843 PubMed ID: 11379776

TITLE: Characteristics of tissue distribution of various polysaccharides as drug carriers: influences of **molecular weight** and anionic charge on tumor targeting.

AUTHOR: Sugahara S; Okuno S; Yano T; Hamana H; Inoue K

CORPORATE SOURCE: Drug Deliver System Institute, Ltd., Noda, Chiba, Japan.. sugawara.sb@om.asahi-kasei.co.jp

SOURCE: BIOLOGICAL AND PHARMACEUTICAL BULLETIN, (2001 May) 24 (5) 535-43.
Journal code: 9311984. ISSN: 0918-6158.

PUB. COUNTRY: Japan

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200109

ENTRY DATE: Entered STN: 20011001

Searcher : Shears 308-4994

Last Updated on STN: 20011001
Entered Medline: 20010927

AB Using the Walker 256 model for carcinosarcoma-bearing rats, we intravenously administered 5 polysaccharide carriers with various **molecular weights** (**MWs**) and electric charges and tested for their plasma and tissue distribution. Two carriers, carboxymethylated-D-manno-D-glucan (CMMG) and CMdextran (CMDex), showed higher plasma AUC than the other carriers tested, namely, CMchitin (CMCh), N-desulfated N-acetylated heparin (DSH), and **hyaluronic** acid (**HA**). This was consistently found to be true over the range of **MWs** tested. For CMDex, the maximum value of plasma AUC was obtained when the **MW** exceeded 150 **kDa**. As for the anionic charge, CMDex (110-180 **kDa**) with a degree of substitution (DS) of the CM groups ranging from 0.2 to 0.6, showed maximum plasma AUC values. Twenty-four hours after administration, the concentration of CMDex (180-250 **kDa**; DS: 0.6-1.2) in tumors was more than 3% of dose/g--approximately 10-fold higher than those observed with CMCh, DSH and **HA**. Doxorubicin (DXR) was **bound** to these **carriers** via a **peptide** spacer, GlyGlyPheGly (GGFG), to give **carrier**-GGFG-DXR **conjugates** (DXR content: 4.2-7.0 (w/w)%), and the antitumor effects of these **conjugates** were tested with Walker 256 carcinosarcoma-bearing rats by monitoring the tumor weights after a single intravenous injection. Compared with free DXR, CMDex-GGFG-DXR and CMMG-GGFG-DXR **conjugates** significantly suppressed tumor growth, while the CMCh-GGFG-DXR, DSH-GGFG-DXR, and **HA** -GGFG-DXR **conjugates** in a similar comparison showed weak tumor growth inhibition. These findings suggest that the antitumor effect of the carrier-DXR **conjugates** was related to the extent with which the carriers accumulated in the tumors.

L15 ANSWER 3 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-681105 [67] WPIDS
DOC. NO. CPI: C2000-207282
TITLE: Compositions to deliver compounds into cells e.g. to treat rheumatoid arthritis, comprise organic halide, targeting ligand and nuclear localization sequence in combination with compound and carrier.

DERWENT CLASS: A96 B07 D16
INVENTOR(S): MCCREERY, T; SADEWASSER, D A; UNGER, E C
PATENT ASSIGNEE(S): (IMAR-N) IMARX PHARM CORP
COUNTRY COUNT: 25
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1046394	A2	20001025	(200067)*	EN	78

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1046394	A2	EP 2000-303249	20000418

PRIORITY APPLN. INFO: US 1999-294623 19990419
AN 2000-681105 [67] WPIDS
AB EP 1046394 A UPAB: 20001223
NOVELTY - Compositions for delivering compounds into cells comprise: an organic halide; a targeting ligand; and a nuclear localization sequence in combination with the compound to be delivered.

ACTIVITY - Immunoregulatory; anti-inflammatory; anti-arthritic.

USE - The compositions are used to deliver compounds into cells (claimed), particularly for the treatment of autoimmune disorders and inflammatory conditions such as rheumatoid arthritis. They may also be used to deliver pharmaceuticals, drugs, diagnostic agents, synthetic organic molecules, peptides, proteins, vitamins, steroids, genetic materials and other bioactive agents e.g. mitotic inhibitors (vinca alkaloids), radiopharmaceuticals (radioactive iodine, phosphorus and cobalt isotopes), hormones (progestins, estrogens, anti-estrogens), anthelmintics, antimalarials, antituberculotics, biologicals (immune sera, antitoxins, antivenoms), rabies prophylactic products, bacterial vaccines, viral vaccines, aminoglycosides, respiratory products (xanthine derivatives, theophylline, aminophylline), thyroid therapeutics (iodine salts, antithyroid agents), cardiovascular products (chelating agents, mercurial diuretics, cardiac glycosides), glucagons, blood products (parenteral iron, hemin, hematoporphyrins and derivatives), targeting ligands (peptides, antibodies, antibody fragments), biological response modifiers (muramyl dipeptide, muramyl tripeptide, microbial cell wall components, lymphokines - bacterial endotoxin e.g. lipopolysaccharide and macrophage activation factor), subunits of bacteria (Mycobacteria, Comebacteria), synthetic dipeptides (N-acetyl-muramyl-L-alanyl-D-isoglutamine), antifungals (ketoconazole, nystatin, griseofulvin, flucytosine, miconazole, amphotericin B), toxins (ricin), immunosuppressants (cyclosporins), antibiotics (beta -lactam, sulfazecin), hormones (growth hormone, melanocyte-stimulating hormone, estradiol, beclomethasone dipropionate, betamethasone, betamethasone acetate, betamethasone sodium phosphate, betamethasone disodium phosphate, cortisone acetate, dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, flunisolide, hydrocortisone, hydrocortisone acetate, hydrocortisone cypionate, hydrocortisone sodium phosphate, hydrocortisone sodium succinate, methylprednisolone, methylprednisolone acetate, methylprednisolone sodium succinate, paramethasone acetate, prednisolone acetate, prednisolone sodium phosphate, prednisolone tebutate, prednisone, triamcinolone, triamcinolone acetonide, triamcinolone diacetate, triamcinolone hexacetonide, fluorocortisone acetate, oxytocin, vasopressin and their derivatives), vitamins (cyanocobalamin neionic acid), retinoids and their derivatives (retinal palmitate, alpha -tocopheryl), peptides and enzymes (manganese superoxide dismutase, alkaline phosphatases), anti-allergens (amelexanox), anticoagulants (phenprocoumon, heparin), tissue plasminogen activators, streptokinase and urokinase), circulatory drugs (propranolol), metabolic potentiators (glutathione), antibiotics (p-aminosalicylic acid, isoniazid, capreomycin sulfate, cycloserine, ethambutol hydrochloride, ethionamide, pyrazinamide, rifampicin, streptomycin sulfate dapsone, chloramphenicol, neomycin, ceflacor, cefadroxil, cephalexin, cephadrine erythromycin, clindamycin, lincomycin, amoxicillin, ampicillin, bacampicillin, carbenicillin, dicloxicillin, cyclacillin, picloxicillin, hetacillin, methicillin, nafcillin, oxacillin, penicillin (G and V), ticarcillin, rifampin,

tetracycline), antivirals (acyclovir, ddI, foscarnet, zidovudine, ribavirin, vidarabine monohydrate), antianginals (diltiazem, nifedipine, verapamil, erythritol tetranitrate, isosorbide dinitrate, nitroglycerin (glyceryl trinitrate), pentaerythritol tetranitrate, anti-inflammatories (difluisal, ibuprofen, indomethacin, meclofenamate, mefenamic acid, naproxen, oxyphenbutazone, phenylbutazone, piroxicam, sulindac, tolmetin, aspirin, salicylates), antiprotozoans (chloraquine, hydroxychloraquine, metronidazole, quinine, meglumine antimonate), antirheumatics (penicillamine), narcotics (paregoric), opiates (codeine, heroin, methadone, morphine, opium), cardiac glycosides (deslanoside, digitoxin, digoxin, digitalin, digitalis), neuromuscular blockers (atracurium mesylate, gallamine triethiodide, hexafluorenium bromide, metrocurine iodide, pancurium bromide, succinylcholine chloride (suxamethionium chloride), tubocurarine chloride, vencuronium bromide), sedatives (amobarbital, amobarbital sodium, aprobarbital, butabarbital sodium, chloral hydrate, ethchlorvynol, ethinamate, flurazepam hydrochloride, glutethimide, methotrimeprazine hydrochloride, methyprylon, midazolam hydrochloride, paraldehyde, pentobarbital, pentobarbital sodium, secobarbital sodium, thiopental sodium), antineoplastics (methotrexate, fluorouracil, adriamycin, mitomycin, ansamitomycin, bleomycin, cysteine arabinoside, arabinosyl adenine, mercaptopolylysine, vincristine, busulfan, chlorambucil, azidothymidine, melphalan (e.g. PAM, L-PAM or phenylalanine mustard), mercaptopurine, mitotane, procarbazine hydrochloride, dactinomycin (actinomycin D), daunorubicin hydrochloride, dosorubicin hydrochloride, Taxol (RTM: paclitaxel), plicamycin (mithramycin), aminoglutethimide, estramustine phosphate sodium, flutamide, leuprolide acetate, megestrol acetate, tamoxifen citrate, testolactone, trilostane, amsacrine (m-AMSA), asparaginase, etoposide (VP-16), interferon alpha -2a, interferon alpha -2b, teniposide (VM-26), vinblastine sulfate (VLB), vincristine sulfate, hydroxyurea, procarbaxine or dacarbazine).

ADVANTAGE - The compositions provide improved delivery of compositions including drugs and genetic materials into cells. They provide for specific targeting and delivery of compounds to particular cells and increased targeting to the nuclei of targeted cells. They also allow delivery to cell lines that would be otherwise resistant to intracellular delivery and gene expression using other conventional means.

DESCRIPTION OF DRAWING(S) - Schematic representation of a targeted composition.

targeted composition 1
lipid coating 2
lipids 2A
halocarbon gas or liquid 3
genetic material 4
targeting ligand 5
lipid head group 6
tether 7
tether 7A
nuclear localization sequence 8
condensing agent. 9

Dwg.2/2

L15 ANSWER 4 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-507223 [46] WPIDS

DOC. NO. CPI: C2000-152167
TITLE: Composition containing hydrophobically modified hedgehog protein, useful for inducing repair of e.g. bone and cartilage, formulated with biodegradable **protein carrier**.

DERWENT CLASS: B04
INVENTOR(S): LANG, K; PAPADIMITRIOU, A
PATENT ASSIGNEE(S): (HOFF) ROCHE DIAGNOSTICS GMBH; (CURI-N) CURIS INC
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1025861	A1	20000809	(200046)*	GE	14
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
WO 2000045848	A1	20000810	(200046)	EN	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000024412	A	20000825	(200059)		
EP 1150716	A1	20011107	(200168)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1025861	A1	EP 1999-101643	19990204
WO 2000045848	A1	WO 2000-EP847	20000203
AU 2000024412	A	AU 2000-24412	20000203
EP 1150716	A1	EP 2000-902654	20000203
		WO 2000-EP847	20000203

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000024412	A	Based on	WO 200045848
EP 1150716	A1	Based on	WO 200045848

PRIORITY APPLN. INFO: EP 1999-101643 19990204
AN 2000-507223 [46] WPIDS
AB EP 1025861 A UPAB: 20000921
NOVELTY - A pharmaceutical composition (A) comprises a hydrophobically modified hedgehog **protein** (I) and, as **carrier**, a biodegradable **protein** (II).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method for preparing (A); and
(2) a method for sustained release of (I) in the human body by administration of (A).
ACTIVITY - Osteogenic; chondrogenic; neurological.
MECHANISM OF ACTION - (I) promote the activity and/or

expression of alkaline phosphatase.
USE - (A) are particularly used for repair of bone and cartilage defects but can also be used for repairing neuronal defects and for systemic delivery of (I).
ADVANTAGE - (II) reversibly **bind** to (I) in its active, folded form and releases it, locally in vivo, in its active state, especially over a period of at least 14 hr. (A) do not induce immunogenic or inflammatory reactions. Lipophilic modification of (I) improves interaction with the lipid membrane of eukaryotic cells.
Dwg.0/2

L15 ANSWER 5 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-367955 [32] WPIDS
DOC. NO. CPI: C2000-111292
TITLE: Novel osteogenetic peptides useful for the treatment and prevention of fractures.

DERWENT CLASS: B04
INVENTOR(S): NISHIMURA, Y; SUZUKI, Y; TANIHARA, M
PATENT ASSIGNEE(S): (KYOC) KYOCERA CORP; (NISH-I) NISHIMURA Y; (SUZU-I) SUZUKI Y; (TANI-I) TANIHARA M

COUNTRY COUNT: 26
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1006126	A2	20000607	(200032)*	EN	22
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2000143697 A		20000526	(200033)		12

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1006126	A2	EP 1999-402815	19991112
JP 2000143697 A		JP 1998-322075	19981112

PRIORITY APPLN. INFO: JP 1998-322075 19981112
AN 2000-367955 [32] WPIDS
AB EP 1006126 A UPAB: 20000706
NOVELTY - Novel peptides chosen from any of the eight peptide sequences, (I)-(VIII),18-22 amino acid (aa) residues in length.
DETAILED DESCRIPTION - Novel peptides chosen from any of the eight following peptide sequences, (I)-(VIII):
(I) Asn-Ser-Val-Asn-Ser-Xaa1-Xaa2-Pro-Lys-Xaa3 -Cys-Cys-Xaa4-Pro-Thr-Glx-Leu-Xaa5-Ala-Ile;
(II) Asn-Ser-Val-Asn-Ser-Xaa1-Xaa2-Pro-Lys-Xaa3 -Cys-Cys-Xaa4-Pro-Thr-Glx-Leu-Xaa5-Ala-Ile-Ser;
(III) Asn-Ser-Val-Asn-Pro-Glu-Xaa1-Xaa2-Pro-Lys-Xaa3-Cys-Cys-Xaa4-Pro-Thr-Glx-Leu-Xaa5-Ala-Ile;
(IV) Asn-Ser-Val-Asn-Pro-Glu-Xaa1-Xaa2-Pro-Lys-Xaa3-Cys-Cys-Xaa4-Pro-Thr-Glx-Leu-Xaa5-Ala-Ile-Ser;
(V) Ile-Asn-Ser-Xaa1-Xaa2-Pro-Lys-Xaa3-Cys-Cys-Xaa4-Pro-Thr-Glx-Leu-Xaa5-Ala-Ile;
(VI) Ile-Asn-Ser-Xaa1-Xaa2-Pro-Lys-Xaa3-Cys-Cys-Xaa4-Pro-Thr-Glx-Leu-Xaa5-Ala-Ile-Ser;

(VII) Ile-Asn-Pro-Glu-Xaa1-Xaa2-Pro-Lys-Xaa3-Cys-Cys-Xaa4-Pro-Thr-Glx-Leu-Xaa5-Ala-Ile; and
(VIII) Ile-Asn-Pro-Glu-Xaa1-Xaa2-Pro-Lys-Xaa3-Cys-Cys-Xaa4-Pro-Thr-Glx-Leu-Xaa5-Ala-Ile-Ser.
Where, Xaa1 = Lys, Ser or Thr;
Xaa2= Ile or Val;
Xaa3= Ala or Pro;
Xaa4= Ala or Val;
Xaa5= Ser or Asn; and
Glx = Glutamine or Glutamate.
INDEPENDENT CLAIMS are also included for the following:
(1) novel peptides chosen from the peptide sequences, (IX)-(X), both 20 (aa) residues in length:
(a) Asn-Ser-Val-Asn-Ser-Lys-Ile-Pro-Lys-Ala-Cys-Cys-Val-Pro-Thr-Glu-Leu-Ser-Ala-Ile (IX); and
(b) Asn-Ser-Val-Asn-Ser-Ser-Ile-Pro-Lys-Ala-Cys-Cys-Val-Pro-Thr-Glu-Leu-Ser-Ala-Ile (X);
(2) an osteogenetic accelerator (A) containing a peptide (I)-(VIII) as an active ingredient; and
(3) an osteogenetic accelerator (B) containing a peptide (IX)-(X) where the **peptide** is fixed to a **carrier**
;

ACTIVITY - Osteogenic; vulnerary; rheumatic.
MECHANISM OF ACTION - Accelerates the activation of alkaline phosphatase in osteoblasts to form neogenetic bone or induces growth of existing bone. An osteogenetic accelerator was implanted in deficient sites of 7mm diameter artificially formed in mandibles of 6 month old female beagles (Nippon SLC). 2 weeks after implantation, tissue including the implant sites was taken out and subjected to tissue staining. Formation of neogenetic bone was clearly observed. For comparison, a sponge-like gel not having the peptide fixed on to it was implanted on the opposite side of the identical dogs, where no neogenetic bone was recognized at all.

ADVANTAGE - The peptides of the invention are negligible in cytoxicity and systemic acute toxicity.
Dwg.0/0

L15 ANSWER 6 OF 40 MEDLINE
ACCESSION NUMBER: 2001053022 MEDLINE
DOCUMENT NUMBER: 20536394 PubMed ID: 11083769
TITLE: Protective and nonprotective epitopes from amino termini of M proteins from Australian aboriginal isolates and reference strains of group A streptococci.
AUTHOR: Brandt E R; Teh T; Relf W A; Hobb R I; Good M F
CORPORATE SOURCE: Cooperative Research Centre for Vaccine Technology, Queensland Institute of Medical Research, and the Australian Centre for International and Tropical Health and Nutrition, University of Queensland, PO Royal Brisbane Hospital, Queensland, Australia.
SOURCE: INFECTION AND IMMUNITY, (2000 Dec) 68 (12) 6587-94. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322
Entered Medline: 20001213

AB The M protein is the primary vaccine candidate to prevent **group A streptococcal** (**GAS**) infection and the subsequent development of rheumatic fever (RF). However, the large number of serotypes have made it difficult to design a vaccine against all strains. We have taken an approach of identifying amino-terminal M protein epitopes from **GAS** isolates that are highly prevalent in **GAS**-endemic populations within the Northern Territory (NT) of Australia. Australian Aboriginals in the NT experience the highest incidence of RF worldwide. To develop a vaccine for this population, 39 peptides were synthesized, representing the amino-terminal region of the M protein from endemic **GAS**. Mice immunized with these peptides **covalently linked** to tetanus toxoid and emulsified in complete Freund's adjuvant raised high-titer antibodies. Over half of these sera reduced bacterial colony counts by >80% against the homologous isolate of **GAS**. Seven of the peptide antisera also cross-reacted with at least three other heterologous peptides by enzyme-**linked** immunosorbent assay. Antiserum to one peptide, BSA10(1-28), could recognize six other peptides, and five of these peptides could inhibit opsonization mediated by BSA10(1-28) antiserum. Cross-opsonization studies showed that six of these sera could opsonize at least one heterologous isolate of **GAS**. These data reveal vaccine candidates specific to a **GAS**-endemic area and show the potential of some to cross-opsonize multiple isolates of **GAS** . This information will be critical when considering which epitopes may be useful in a multiepitope vaccine to prevent **GAS** infection.

L15 ANSWER 7 OF 40 MEDLINE
ACCESSION NUMBER: 2000418214 MEDLINE
DOCUMENT NUMBER: 20290244 PubMed ID: 10832647
TITLE: Localization and characterization of the ligand-binding domain of the fibrinogen-binding protein (FgBP) of Streptococcus equi subsp. equi.
AUTHOR: Meehan M; Muldowney D A; Watkins N J; Owen P
CORPORATE SOURCE: National Pharmaceutical Biotechnology Centre, BioResearch, Ireland, Dublin.
SOURCE: MICROBIOLOGY, (2000 May) 146 (Pt 5) 1187-94. Journal code: 9430468. ISSN: 1350-0872.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000907

AB The **group C streptococcus** **Streptococcus** equi subsp. equi possesses a 498-residue major cell-wall-associated protein (FgBP) which **binds** horse fibrinogen (Fg), reacts with convalescent horse serum and protects against lethal S. equi challenge in a small animal model. In the present study, analysis of a panel of 17 purified N- and C-terminal FgBP truncates by ligand affinity blotting and SDS-PAGE revealed that the region required for maximum **binding** of Fg

extended over the first half of the mature protein. The C-terminal two-thirds of this domain is predicted to be alpha-helical coiled-coil and the N-terminal one-third to possess non-coiled-coil single strands. Residues at the extreme N-terminus and within the coiled-coil region are both required for ligand **binding**. A high incidence of alpha-helical coiled-coil structure also seems to be responsible in part for the aberrant mobility of FgBP on SDS gels. The efficiency with which FgBP **binds** Fg from different animal species decreases in the order horse > mouse, pig > rat > sheep, dog, bovine, human. **Binding** to horse Fg is inversely related to temperature over the range 45-4 degrees C and is independent of Ca2+ ions. MS analysis provided corroborative evidence that FgBP is **covalently linked** to the cell wall peptidoglycan.

L15 ANSWER 8 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1995-224081 [29] WPIDS
CROSS REFERENCE: 1999-180035 [15]
DOC. NO. CPI: C1995-103061
TITLE: Compsns. comprising **hyaluronate** functionalised with di hydrazide - useful in biological, medical, surgical and cosmetic applications.
DERWENT CLASS: A96 B04 D21
INVENTOR(S): POUYANI, T; PRESTWICH, G D
PATENT ASSIGNEE(S): (UYNY) UNIV NEW YORK STATE RES FOUND
COUNTRY COUNT: 57
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9515168	A1	19950608	(199529)*	EN	65
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ					
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KE KG KP KR KZ LK LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA UZ VN					
AU 9512602	A	19950619	(199540)		
US 5616568	A	19970401	(199719)		24
US 5652347	A	19970729	(199736)		22

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9515168	A1		WO 1994-US13580	19941123
AU 9512602	A		AU 1995-12602	19941123
US 5616568	A		US 1993-158996	19931130
US 5652347	A	Div ex	US 1993-158996	19931130
			US 1995-484567	19950607

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9512602	A	Based on	WO 9515168

PRIORITY APPLN. INFO: US 1993-158996 19931130; US 1995-484567

19950607

AN 1995-224081 [29] WPIDS
CR 1999-180035 [15]
AB WO 9515168 A UPAB: 19990416
Compsn. of matter comprises a **hyaluronate** functionalised with a dihydrazide.

Prepn. of functionalised **hyaluronate** gels is also claimed.

The dihydrazide is esp. of formula H2N-NH-CO-A-CO-NH-NH2 (I). A = (un)substd. hydrocarbyl or heterohydrocarbyl of 0-20 carbons or heteroatoms (esp. N, O or S).

The compsn. may also comprise at least one additional component (e.g. **covalently** bonded to an amine gp. of the dihydrazide) such as a fatty acid, topical medicament, perfume, UV absorbing agent, or drug (e.g. an antiinflammatory, antiviral, antifungal or antiproliferative agent.

Functionalised **hyaluronate** gels may be prepd. by: (a) mixing **hyaluronate** with a dihydrazide in an aq. soln. to form a **hyaluronate**-dihydrazide mixt.; (b) adding a carbodiimide to the mixt.; and (c) allowing the mixt. to react in the presence of carbodiimide under conditions which produce **hyaluronate** functionalised with dihydrazide.

USE - The compsns. form biocompatible gels or hydrogels and can serve as intermediates for attachment of bio-effecting agents, drugs, **peptides**, fluorocarbons, cosmetic agents, oxygen **carriers**, etc.

The compsns. may be administered to humans or animals, parenterally or topically.

ADVANTAGE - The prepn. of modified **hyaluronic** acid does not compromise the mol. wt. of the **HA** molecule, can be irreversible or reversible, provides a pendant functional gp. which can act as a versatile **coupling** site and gives gels with a strength and type which can be easily manipulated.

Dwg.0/4

ABEQ US 5616568 A UPAB: 19970512
A composition of matter comprising **hyaluronate** functionalised with a dihydrazide at **glucuronic** acid sites of the **hyaluronate**.

Dwg.0/0

ABEQ US 5652347 A UPAB: 19970909
A method for making a functionalised **hyaluronate** gel comprising;

(i) mixing **hyaluronate** with a dihydrazide in a substantially aqueous solution to form a **hyaluronate** -dihydrazide mixture;

(ii) adding a carbodiimide to the **hyaluronate** -dihydrazide mixture; and

(iii) allowing the **hyaluronate**-dihydrazide mixture to react in the presence of carbodiimide under conditions producing **hyaluronate** functionalised with dihydrazide.

Dwg.0/4

L15 ANSWER 9 OF 40 MEDLINE
ACCESSION NUMBER: 95123446 MEDLINE
DOCUMENT NUMBER: 95123446 PubMed ID: 7529827
TITLE: Requirement of the hyaluronan receptor RHAMM in neurite extension and motility as demonstrated in primary neurons and neuronal cell lines.

AUTHOR: Nagy J I; Hacking J; Frankenstein U N; Turley E A
CORPORATE SOURCE: Department of Physiology, University of Manitoba, Winnipeg, Canada.
SOURCE: JOURNAL OF NEUROSCIENCE, (1995 Jan) 15 (1 Pt 1) 241-52.
Journal code: 8102140. ISSN: 0270-6474.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950223
Last Updated on STN: 19960129
Entered Medline: 19950214

AB The recently cloned and characterized **hyaluronan** (**HA**) receptor RHAMM (receptor for **HA**-mediated motility) **has** been shown to play a critical role in mechanisms underlying the motile capacity of a variety of peripheral cell types. Similarities in molecular processes that govern cell locomotion and growth cone migration prompted us to investigate whether RHAMM also contributes to neurite migration in vitro. In immunohistochemical studies of PC12 cells, NG108-15 cells and a neuroblastoma/spinal cord neuronal hybrid cell line (NSC-34 cells) as well as rat and human primary neurons, a punctiform RHAMM labeling pattern was detected in cell bodies, along processes, and at growth cones. By Western blot analysis, the cells lines expressed major RHAMM forms with apparent **MW** of 60, 75, and 116 **kDa**. Treatment of NG108-15 cells with dibutyryl-cAMP led to a clear increase in immunolabeling for RHAMM and enhanced expression of the 60 and 75 **kDa** forms. A polyclonal anti-RHAMM antibody that interferes with **HA**/RHAMM interaction significantly reduced neurite migration of each cell type examined, while another directed against a RHAMM repeat sequence thought to promote RHAMM receptor aggregation significantly stimulated neurite migration of NSC-34 and rat primary neurons. Different monoclonal anti-RHAMM antibodies had differential inhibitory actions on neurite movement. Low concentrations (ng/ml) of a peptide corresponding to an **HA binding** domain within RHAMM inhibited neurite migration. These results are the first to implicate RHAMM in the mediation of neurite motility and migration and to point to the potential importance of **HA** in this process.

L15 ANSWER 10 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1994-248890 [30] WPIDS
DOC. NO. CPI: C1994-113189
TITLE: Promoting repair and attachment of cartilaginous tissue - using e.g. new fusion polypeptide of **link** protein and cartilage matrix protein, partic. for treating damage caused by arthritis.
DERWENT CLASS: B04
INVENTOR(S): BINETTE, F; GOETINCK, P F; TONDRAVI, M M; TONDRAVI, M
PATENT ASSIGNEE(S): (GEHO) GEN HOSPITAL CORP
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 9415627 A1 19940721 (199430)* EN 48
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 9462284 A 19940815 (199442)
EP 679089 A1 19951102 (199548) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 679089 A4 19960529 (199644)
JP 08507205 W 19960806 (199702) 43
US 5872094 A 19990216 (199914)
US 5986052 A 19991116 (200001)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9415627	A1		WO 1994-US253	19940104
AU 9462284	A		AU 1994-62284	19940104
EP 679089	A1		EP 1994-909439	19940104
			WO 1994-US253	19940104
			EP 1994-909439	
EP 679089	A4		JP 1994-516236	19940104
JP 08507205	W		WO 1994-US253	19940104
			US 1993-1078	19930106
US 5872094	A		US 1993-1078	19930106
US 5986052	A	Div ex	US 1995-463218	19950605

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9462284	A	Based on	WO 9415627
EP 679089	A1	Based on	WO 9415627
JP 08507205	W	Based on	WO 9415627
US 5986052	A	Div ex	US 5872094

PRIORITY APPLN. INFO: US 1993-1078 19930106; US 1995-463218
19950605

AN 1994-248890 [30] WPIDS
AB WO 9415627 A UPAB: 19940914
Repair of diseased or injured cartilaginous tissue is promoted by treating the tissue with a polypeptide (I) that promotes **binding** of a complex (C) of proteoglycan (PG) and **hyaluronic** acid (**HA**) to collagen.

(I) esp. comprises the CMP-1 or -2 homologous repeat sequences attached to intact LP. In method (1), anchorage includes attaching cells (esp. chondrocytes) contg. recombinant nucleic acid able to express one of the specified polypeptides on its surface. In method (5), the polypeptide is esp. CMP (or its fragment able to **bind** to collagen and LP) or FP. The non-cartilaginous tissue is partic. skin and the polypeptide is expressed by transformed fibroblasts.

USE - (I) are used to treat cartilage in joints, esp. where damage has been caused by arthritis (specifically osteoarthritis), or to promote cartilage matrix formation in vitro to provide material for restorative or cosmetic surgery. It also promotes attachment to prostheses, implants, tissue grafts, etc. CMP polypeptides can be used cosmetically to improve tissue hydration, while CMP, LP and (I) can be used as **carriers** for other

(usually **covalently** attached) **proteins.**
Dwg.0/5

L15 ANSWER 11 OF 40 MEDLINE
ACCESSION NUMBER: 95155671 MEDLINE
DOCUMENT NUMBER: 95155671 PubMed ID: 7531724
TITLE: A sulfated proteoglycan as a novel ligand for CD44.
AUTHOR: Toyama-Sorimachi N; Miyasaka M
CORPORATE SOURCE: Department of Immunology, Tokyo Metropolitan Institute of Medical Science, Japan.
SOURCE: JOURNAL OF DERMATOLOGY, (1994 Nov) 21 (11) 795-801. Journal code: 7600545. ISSN: 0385-2407.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950322
Last Updated on STN: 19960129
Entered Medline: 19950314

AB We have identified a novel ligand for CD44, a cell surface glycoprotein implicated in tumor metastasis and lymphocyte homing. When the mouse T cell line CTLL-2 was transfected with cDNA encoding a hemopoietic form of mouse CD44, CTLL-2 cells exhibited a new self-adhesive phenotype, forming large aggregates. The aggregation was blocked by neutralizing anti CD44 monoclonal antibody but unaffected by hyaluronidase, indicating the involvement of CD44 and its non-**hyaluronate** ligand in the cell aggregation. The ability to induce CD44-dependent aggregation was found in culture supernatants of CTLL-2 and its CD44 transfectants. The use of CD44-immunoglobulin chimeric protein revealed that CTLL-2 and its transfectants synthesized a large-**molecular weight** protein (gp600) which **bound** specifically to CD44. The gp600 was readily labeled with radioactive sulfate, and treatment of gp600 with chondroitinase ABC or ACII generated a lower **molecular weight** species (18-22 **kDa**), suggesting that gp600 consists of a small core protein with chondroitin sulfate glycosaminoglycan side chains. However, **binding** of CD44 to glycosaminoglycans such as chondroitin 4-sulfate, chondroitin 6-sulfate, and dermatan sulfate was undetectable, suggesting either that a novel chondroitin-type glycosaminoglycan is recognized by CD44 or that a particular configuration of the glycosaminoglycan is required for recognition by CD44.

L15 ANSWER 12 OF 40 MEDLINE
ACCESSION NUMBER: 95212481 MEDLINE
DOCUMENT NUMBER: 95212481 PubMed ID: 7535241
TITLE: Receptors for hyaluronan on corneal endothelial cells.
AUTHOR: Forsberg N; Von Malmborg A; Madsen K; Rolfsen W; Gustafson S
CORPORATE SOURCE: Department of Medical and Physiological Chemistry, University of Uppsala, Sweden.
SOURCE: EXPERIMENTAL EYE RESEARCH, (1994 Dec) 59 (6) 689-96. Journal code: 0370707. ISSN: 0014-4835.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950510
Last Updated on STN: 19960129
Entered Medline: 19950503

AB Previous investigations suggest that the corneal endothelium **has** specific **binding** sites for **hyaluronan** (HYA). In the present study, biochemical and immunological techniques were used to characterize these **binding** sites and to compare them with the liver endothelial cell (LEC) HYA receptor. Affinity chromatography of solubilised, 125I-labelled corneal endothelial cell surface proteins on immobilised HYA proved that there were molecules that were strongly **bound** to the polysaccharide. A part of these molecules formed a 100-**kDa** band when analysed by autoradiography after SDS polyacrylamide electrophoresis (PAGE). A specific antibody against the rat LEC HYA receptor was used for immunohistochemical studies of monkey and human corneas. There was a specific staining of the corneal endothelium of both species, and **hyaluronan** treatment before isolation of the human eyes reduced the staining intensity. Hyaluronidase treatment of the tissue sections before receptor staining strikingly increased the specific staining of the corneal endothelial cells (CEC). Immunoblotting of human corneal proteins, separated by SDS-PAGE, showed staining at 200, 150-160 and 55 **kDa**. Uptake experiments of tritiated HYA in cultured monkey CEC showed only a slight increase in cell associated radioactivity over 2-6 hr. The results make it unlikely that the corneal endothelial receptor, like its liver endothelial counterpart, is actively involved in receptor-mediated endocytosis. Our studies suggest that CEC carry receptors for HYA that are immunologically similar to the LEC receptors. CEC receptors might act as **binding** structures increasing the concentration of HYA close to the CEC as a protection of these vulnerable cells from physicochemical damage.

L15 ANSWER 13 OF 40 MEDLINE
ACCESSION NUMBER: 94289347 MEDLINE
DOCUMENT NUMBER: 94289347 PubMed ID: 7517179
TITLE: A novel ligand for CD44 is sulfated proteoglycan.
AUTHOR: Toyama-Sorimachi N; Miyasaka M
CORPORATE SOURCE: Department of Immunology, Tokyo Metropolitan Institute of Medical Science, Japan.
SOURCE: INTERNATIONAL IMMUNOLOGY, (1994 Apr) 6 (4) 655-60. Journal code: 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940815
Last Updated on STN: 19960129
Entered Medline: 19940804

AB We report herein identification of a novel ligand for CD44, a cell surface glycoprotein implicated in tumor metastasis, lymphocyte differentiation and homing. A mouse T cell line CTLL-2 transfected with cDNA encoding a hemopoietic form of mouse CD44 exhibited a new self-adhesive phenotype, forming large aggregates. The aggregation

was blocked by anti-CD44 mAb but little affected by hyaluronidase, indicating the involvement of CD44 and its non-**hyaluronate** ligand in the cell aggregation. The ability to induce CD44-dependent aggregation was observed in culture supernatants of CTLL-2 and its CD44 transfectants. Immunoprecipitation analysis using a CD44-Ig chimeric molecule indicated that CTLL-2 and its transfectants synthesized a macromolecule (gp600) which **bound** specifically to CD44. gp600 was readily labeled with radioactive sulfate and treatment of gp600 with chondroitinase ABC or AC II generated a lower **molecular weight** species (18-22 **kDa**), suggesting that gp600 consists of a small core protein heavily modified with chondroitin sulfate glycosaminoglycan side chains. However, when **binding** of CD44 was tested in vitro to chondroitinase-sensitive purified glycosaminoglycans, such as chondroitin-4-sulfate, chondroitin-6-sulfate and dermatan sulfate, no **binding** was demonstrable, suggesting either that a novel type of chondroitinase-sensitive glycosaminoglycan is recognized by CD44 or that association of the glycosaminoglycan with a core protein is required for recognition by CD44.

L15 ANSWER 14 OF 40 MEDLINE
ACCESSION NUMBER: 95035186 MEDLINE
DOCUMENT NUMBER: 95035186 PubMed ID: 7524689
TITLE: Biotinylated hyaluronic acid: a new tool for probing hyaluronate-receptor interactions.
AUTHOR: Pouyani T; Prestwich G D
CORPORATE SOURCE: Department of Chemistry, University at Stony Brook, New York 11794-3400.
SOURCE: BIOCONJUGATE CHEMISTRY, (1994 Jul-Aug) 5 (4) 370-2. Journal code: 9010319. ISSN: 1043-1802.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19960129
Entered Medline: 19941223

AB **Hyaluronic** acid (**HA**) is a linear polysaccharide composed of repeating disaccharide units of D-**glucuronic** acid (GlcUA) and N-acetyl-D-glucosamine (GlcNAc). **Hyaluronate** plays an important role in many biological processes as mediated by its interactions with a number of **HA-binding** proteins (the "hyaladherins") and with the cell surface **HA**-receptor, CD44. Studies of **hyaluronate**-hyaladherin interactions would be greatly facilitated by the availability of molecular probes derived from **HA**. We recently reported a convenient chemical modification of **hyaluronate** that introduces multiple pendant amine functionalities onto the **HA** carboxylate residues. We now report the preparation of biotinylated **hyaluronic** acid (molecular weight = 1.2 x 10(6) Da) as a probe for histochemical and immunochemical characterization of **HA-binding** proteins. Approximately one-third of the available **HA** glucuronate residues could be readily biotinylated in high molecular weight **HA**.

L15 ANSWER 15 OF 40 MEDLINE
ACCESSION NUMBER: 94231212 MEDLINE
DOCUMENT NUMBER: 94231212 PubMed ID: 7513749
TITLE: CD44-**hyaluronate** interaction mediates in vitro lymphocyte **binding** to the white matter of the central nervous system.

AUTHOR: Aho R; Jalkanen S; Kalimo H
CORPORATE SOURCE: Department of Pathology, University of Turku, Finland.

SOURCE: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, (1994 May) 53 (3) 295-302.
Journal code: 2985192R. ISSN: 0022-3069.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940620
Last Updated on STN: 19960129
Entered Medline: 19940609

AB The cell adhesion molecule CD44 is expressed in the central nervous system, especially on glial cells in the white matter, the extracellular matrix of which also contains one of its ligands, **hyaluronate**. We investigated the role of CD44 and **hyaluronate** in the adhesion of human peripheral blood lymphocytes to myelinated areas of cerebellum by an in vitro **binding** assay. Hermes-1 epitope, which recognizes the **hyaluronate binding** site of CD44, and Hermes-3 epitope, involved in lymphocyte **binding** to mucosal high endothelial venules, were both immunohistochemically expressed in the white matter. No immunoreactivity was observed with mAb Var3.1, which sees variant forms of CD44 containing the exon v6 encoding region. The **molecular weight** analysis showed that CD44 of the white matter was identical to the major 90 **kD** form of CD44 present on lymphocytes. The **binding** of both T and B lymphocytes was significantly inhibited by pretreatment of both cells and sections with mAb Hermes-1 but not with Hermes-3. Digestion of the sections and/or lymphocytes with hyaluronidase also reduced lymphocyte **binding**. These findings implicate that CD44-**hyaluronate** mediates lymphocyte adhesion to the white matter and this interaction may be involved in the pathogenesis of inflammations and lymphomas of the central nervous system.

L15 ANSWER 16 OF 40 MEDLINE
ACCESSION NUMBER: 94325116 MEDLINE
DOCUMENT NUMBER: 94325116 PubMed ID: 7519432
TITLE: Evidence for presence of hyaluronan binding protein on spermatozoa and its possible involvement in sperm function.

AUTHOR: Ranganathan S; Ganguly A K; Datta K
CORPORATE SOURCE: Biochemistry Laboratory, School of Environmental Sciences, Jawaharlal Nehru University, New Delhi, India.

SOURCE: MOLECULAR REPRODUCTION AND DEVELOPMENT, (1994 May) 38 (1) 69-76.
Journal code: 8903333. ISSN: 1040-452X.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19940914
Last Updated on STN: 19960129
Entered Medline: 19940902

AB **Hyaluronic** acid, a major component of the extracellular matrix, plays an important role in the regulation of different cellular processes, e.g., locomotion, cell-cell interaction during morphogenesis, and differentiation. Distribution of **hyaluronic** acid with respect to the role of sperm hyaluronidase in sperm penetration and gamete interaction is well established. In order to elucidate this mechanism, in our current study we have identified and demonstrated, for the first time, the presence of a 68-**kDa** cell surface **hyaluronic** acid **binding** glycoprotein (HABP) in spermatozoa of different species (rat, mice, bull, and human) by immunoblot analysis and indirect immunofluorescence using the polyclonal antibodies raised against purified HABP. Furthermore, we were able to demonstrate a differential distribution of 68-**kDa** **HA binding** protein on the sperm head, midpiece, and tail of different species. To identify its role in sperm function, we observed its declining pattern during epididymal maturation and also the inhibition of sperm-oolemmal adherence by pretreatment of the sperms with anti-HABP antibodies. We have further observed its in vivo phosphorylation in motile spermatozoa. All our data clearly indicate that sperm **hyaluronan** **binding** protein may have a specific role in sperm maturation, motility, and fertilization processes.

L15 ANSWER 17 OF 40 MEDLINE
ACCESSION NUMBER: 95146448 MEDLINE
DOCUMENT NUMBER: 95146448 PubMed ID: 7844061
TITLE: On the beta-glucuronidase binding protein (BGBP) of microorganisms. Its purification, the antiserum preparation against that and its localization in leproma and the other infectious lesions shown by immunohistologic method.
AUTHOR: Matsuo E; Komatsu A; Maekawa S; Furuno Y; Matsushita A; Sumiishi A; Sasaki N; Skinsnes O K
CORPORATE SOURCE: Department of Pathology, Kyorin University School of Medicine.
SOURCE: NIPPON RAI GAKKAI ZASSHI. JAPANESE JOURNAL OF LEPROSY, (1994 Jul) 63 (2) 35-46.
Journal code: 7901165. ISSN: 0386-3980.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950316
Last Updated on STN: 19950316
Entered Medline: 19950308

AB Our previous studies suggested that M. leprae (ML) grow in peripheral nerves and lepra cells because ML metabolize **hyaluronic** acid (**HA**), and use its component for their growth by the aid of host enzyme combined to the bacilli

derived beta-glucuronidase **binding** protein (BGBP). In this study, therefore, we examined the method to purify BGBP from a mycobacterium HI-75 originally separated from a leproma and cultured by modified Ogawa's medium containing split products of **HA** (**glucuronic** acid and N-acetylglucosamine). The distribution of BGBP in leproma and the other lesions consisting of hepatitis B virus infected liver and M. avium-intracellulare infected lung tissue were also immunohistologically examined. As the result, the best method to get BGBP was preparatory electrophoresis in the final step of the purification and not the molecular sieving. The BGBP was actually proven in leproma and the other infected tissues as described, indicating the abilities of these microorganisms to utilize the metabolic machinery of the host with the similar ways to that of ML.

L15 ANSWER 18 OF 40 MEDLINE
ACCESSION NUMBER: 94218823 MEDLINE
DOCUMENT NUMBER: 94218823 PubMed ID: 8165568
TITLE: Migration stimulating factor (MSF): its structure, mode of action and possible function in health and disease.
AUTHOR: Schor S L; Grey A M; Ellis I; Schor A M; Coles B; Murphy R
CORPORATE SOURCE: Department of Cell and Structural Biology, University of Manchester, UK.
SOURCE: SYMPOSIA OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY, (1993) 47 235-51. Ref: 49
Journal code: 0404517. ISSN: 0081-1386.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940606
Last Updated on STN: 19940606
Entered Medline: 19940520

AB We have previously reported that (a) fetal fibroblasts migrate into 3-dimensional collagen matrices to a significantly greater extent that do adult cells, (b) this difference in migratory behaviour results from the secretion by fetal fibroblasts of a "migration stimulating factor" (MSF), and (c) adult fibroblasts retain responsiveness to MSF, this providing the basis of a bioassay for monitoring factor activity. Using a recently modified purification protocol, MSF isolated from fetal fibroblast conditioned medium elutes as a single activity peak in the penultimate Mono Q anion exchange chromatography step. Analysis of this material by SDS-PAGE indicates that it consists of three proteins, one with an apparent molecular mass of 119 **kDa** and a doublet with molecular masses of approximately 43 and 33 **kDa**, respectively. Our data suggest that the two proteins comprising the doublet result from the degradation of the larger molecule during the purification procedure. Both the 119 **kDa** species and lower **molecular weight** doublet stimulate fibroblast migration (with half maximal activity in the region of 1-10 pg/ml) and contain a structural domain exhibiting significant amino acid sequence homology with the gelatin-**binding** fragment (GBF)

of fibronectin. Bona fide preparations of GBF, obtained by the limited proteolysis of plasma fibronectin, also stimulate the migration of adult fibroblasts in a similar dose-dependent manner to that of MSF. In spite of this similarity, MSF and GBF differ in terms of a number of biological and biochemical parameters, thereby suggesting that MSF is a distinct gene product and not a proteolytic degradation fragment of fibronectin. MSF stimulates the synthesis of a high **molecular weight** species of **hyaluronic** acid (**HA**). Our current data suggest that the observed effect of MSF on cell migration is actually a secondary consequence of the accumulation of this **HA** in the collagen matrix. TGF-beta is a potent inhibitor of MSF, both in terms of its effects on cell migration and **HA** synthesis. As MSF is present in wound fluid, we have suggested that the inhibition of MSF activity by TGF-beta may reflect the antagonistic interaction of these two cytokines in the control of the wound healing process. Our recent data indicate that discrete minority subpopulations of MSF-secreting fibroblasts are also present at specific sites in the healthy adult and that these may undergo a transient and local expansion during wound healing.(ABSTRACT TRUNCATED AT 400 WORDS)

L15 ANSWER 19 OF 40 MEDLINE
ACCESSION NUMBER: 94363380 MEDLINE
DOCUMENT NUMBER: 94363380 PubMed ID: 7521750
TITLE: A glycoprotein expressed by human fibrous astrocytes is a **hyaluronate-binding** protein and a member of the CD44 family.
AUTHOR: da Cruz L A; Cruz T F; Moscarello M A
CORPORATE SOURCE: Department of Biochemistry, Hospital for Sick Children, Toronto, Ontario, Canada.
SOURCE: CELL ADHESION AND COMMUNICATION, (1993 May) 1 (1) 9-20.
Journal code: 9417027. ISSN: 1061-5385.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941021
Last Updated on STN: 19960129
Entered Medline: 19941010

AB We have isolated and characterized an antigen from normal human brain called p80, so called because it migrated with an M(r) of 80 **kDa** on SDS PAGE. The M(r) of 80 **kDa** consists of a protein of about 55-60 **kDa** and carbohydrate (20-25 **kDa**). The carbohydrate is almost entirely of the N-**linked** type, although a small amount of O-**linked** carbohydrate was detected. Cross-reactivity with monoclonal antibodies A3D8 and A1G3 showed that p80 could therefore be considered an isoform of the CD44 adhesion molecules. In addition, specific **binding** to **hyaluronate** which was not competed for by proteoglycan demonstrated that it involved different sites than the proteoglycan **binding** sites. We also observed that fucoidan and dextran sulphate increased the **binding** by 200-250% while chondroitin sulphate C also increased the **binding** but to a lesser extent. Heparin, heparan sulphate and chondroitin sulphates A and B did not have such

an effect. The **binding** of p80 to **hyaluronate** was pH dependent with a maximum at pH 6.4. We concluded that p80 was an astrocyte specific adhesion molecule.

L15 ANSWER 20 OF 40 MEDLINE
ACCESSION NUMBER: 92251189 MEDLINE
DOCUMENT NUMBER: 92251189 PubMed ID: 1578147
TITLE: Protein Arp and protein H from **group A streptococci**. Ig **binding** and dimerization are regulated by temperature.
AUTHOR: Akerstrom B; Lindahl G; Bjorck L; Lindqvist A
CORPORATE SOURCE: Department of Medical and Physiological Chemistry, University of Lund, Sweden.
SOURCE: JOURNAL OF IMMUNOLOGY, (1992 May 15) 148 (10) 3238-43.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19920619
Entered Medline: 19920609

AB Cell surface proteins that **bind** to the Fc part of Ig are expressed by many strains of **group A streptococci**, an important human pathogen. Two such bacterial strains, AP4 and AP1, were shown to **bind** IgA and IgG, respectively, in a temperature-dependent manner. The **binding** of radiolabeled Ig to the bacterial cells was lower at 37 degrees C than at 22 and 4 degrees C. Similarly, protein Arp, the IgA-**binding** protein isolated from strain AP4, and protein H, the IgG-**binding** protein isolated from strain AP1, displayed a strong Ig-**binding** at 22 degrees C and lower temperatures, and virtually no **binding** at all at 37 degrees C. The effect was reversible: lowering of the temperature restored the **binding** and vice versa. A gradual shift between **binding** and nonbinding took place between 27 and 37 degrees C. Gel chromatography and velocity sedimentation centrifugation showed that protein Arp and protein H appeared as noncovalently associated dimers at 10 and 22 degrees C, and as monomers at 37 degrees C. These results strongly suggest that the dimerization of protein Arp and protein H, rather than the low temperature itself, yielded the strong Ig-**binding** of the proteins at 10 and 22 degrees C. Indeed, after **covalent** cross-**linking** of the dimers at 10 degrees C by incubation with low concentrations of glutaraldehyde, full Ig-**binding** was achieved even at 37 degrees C. A carboxyl-terminal proteolytic fragment of protein Arp, which completely lacked the IgA-**binding** capacity at any temperature, showed the same temperature-dependent dimerization as intact protein Arp, suggesting that the Ig-**binding** part of the protein is not required for dimerization. The implications of these results for the function of Ig-**binding group A streptococcal** proteins, and their role in the host-parasite relationship are discussed.

L15 ANSWER 21 OF 40 MEDLINE

ACCESSION NUMBER: 93129231 MEDLINE
DOCUMENT NUMBER: 93129231 PubMed ID: 1282807
TITLE: Rat hepatocyte hyaluronan/glycosaminoglycan binding proteins: evidence for distinct divalent cation-independent and divalent cation-dependent activities.
AUTHOR: Frost S J; Kindberg G M; Oka J A; Weigel P H
CORPORATE SOURCE: Department of Human Biological Chemistry and Genetics, University of Texas Medical Branch, Galveston 77555-0647.
CONTRACT NUMBER: GM 35978 (NIGMS)
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1992 Dec 30) 189 (3) 1591-7.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302
ENTRY DATE: Entered STN: 19930226
Last Updated on STN: 19970203
Entered Medline: 19930208

AB We have previously shown (Biochemistry, 29, 10425, 1990) that hepatocytes contain intracellular specific **binding** sites for **hyaluronan** (**HA**). Although **HA-binding** activity is not dependent on divalent cations, it is increased in the presence of Ca+2. Here we report that a novel photoaffinity **HA** derivative (ASD-**HA**) crosslinks specifically to different proteins in permeable cells in the presence or absence of Ca+2. With Ca+2 present, two proteins of approximately 24 **kD** and 43 **kD** were labeled. Additionally, a broad zone of specific crosslinking was observed in the region of 40-100 **kD**. However, in the presence of the chelator EGTA this zone was absent and the 24 and 43 **kD** proteins were also not cross-**linked** to the **HA** photoaffinity derivative. In the absence of Ca+2, only a 54 **kD** protein was specifically labeled. The results indicate that different intracellular hepatocyte proteins are responsible for the Ca+2-independent and the Ca+2-dependent **binding** of **HA**.

L15 ANSWER 22 OF 40 MEDLINE
ACCESSION NUMBER: 91282778 MEDLINE
DOCUMENT NUMBER: 91282778 PubMed ID: 1711848
TITLE: Evidence for autophosphorylation of **hyaluronate binding** protein and its enhanced phosphorylation in rat histiocytoma.
AUTHOR: Babu B R; Gupta S; Datta K
CORPORATE SOURCE: Biochemistry Laboratory, School of Environmental Sciences Jawaharlal Nehru University, New Delhi, India.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1991 Jun 28) 177 (3) 1291-8.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19910818
Last Updated on STN: 19970203
Entered Medline: 19910731

AB This report documents for the first time the in vitro autophosphorylation of purified 68 **kDa hyaluronate binding** protein in presence of [32P] ATP. The rate of phosphorylation is proportional to the concentration of protein and to the time of incubation up to 5 min. By both phosphoamino acid and western blot analysis with antiphosphotyrosine antibodies, we have confirmed that the phosphorylation occurs at tyrosine residues. Immunoprecipitation with anti **HA binding** protein antibody shows a 5 fold increase in the phosphorylation in macrophage histiocytoma compared to normal macrophage. Supplementing **hyaluronate** with **hyaluronate binding** protein in the medium is further shown to enhance total protein phosphorylation in rat histiocytoma.

L15 ANSWER 23 OF 40 MEDLINE
ACCESSION NUMBER: 91100024 MEDLINE
DOCUMENT NUMBER: 91100024 PubMed ID: 1987071
TITLE: Binding of a Streptococcus mutans cationic protein to kidney in vitro.
AUTHOR: Choi S H; Stinson M W
CORPORATE SOURCE: Department of Microbiology, School of Medicine and Biomedical Sciences, State University of New York, Buffalo 14214.
CONTRACT NUMBER: RO1-DE05696 (NIDCR)
SOURCE: INFECTION AND IMMUNITY, (1991 Feb) 59 (2) 537-43. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 20000303
Entered Medline: 19910220

AB An 8-kDa protein, with **binding** activity for heparin and heparan sulfate of basal laminae of animal tissues, was isolated from Streptococcus mutans MT703 and purified to homogeneity. **Binding** of radioiodinated 8-kDa protein to rabbit kidney tissue in vitro showed a high degree of specificity, as indicated by saturation kinetics, time dependence, and competitive inhibition by unlabeled protein. **Binding** activity for kidney tissue was competitively inhibited by selected glycosaminoglycans and polyanions in the following order: heparin greater than dextran sulfate greater than heparan sulfate greater than chondroitin sulfate greater than lipoteichoic acid greater than keratan sulfate greater than **hyaluronic** acid. **Binding** of the streptococcal protein to rabbit kidney tissue was also strongly inhibited by protamine sulfate, polylysine, and a random copolymer of lysine and alanine. Among the monosaccharides tested at 50 mM, glucosamine 2,3- or 2,6-disulfate, **glucuronic** acid, glucose 6-phosphate, and glucose 6-sulfate inhibited 50% or more of the **binding** activity, whereas N-acetylglucosamine 3-sulfate, glucosamine 6-sulfate, N-acetyl-glucosamine, N-acetylgalactosamine, N-acetylneuraminic acid, and a selection of

neutral sugars were not inhibitory. The heparin-**binding** protein was detected on the cell wall of S. mutans and in the culture medium following growth. Several other species of streptococci produce an immunologically related protein of similar size.

L15 ANSWER 24 OF 40 MEDLINE

ACCESSION NUMBER: 91311713 MEDLINE
DOCUMENT NUMBER: 91311713 PubMed ID: 1713274
TITLE: Extracellular matrix of central nervous system white matter: demonstration of an hyaluronate-protein complex.
AUTHOR: Asher R; Perides G; Vanderhaeghen J J; Bignami A
CORPORATE SOURCE: Department of Pathology, Harvard Medical School, Boston, Massachusetts.
CONTRACT NUMBER: NS 13034 (NINDS)
SOURCE: JOURNAL OF NEUROSCIENCE RESEARCH, (1991 Mar) 28 (3) 410-21.
Journal code: 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910913
Last Updated on STN: 19990129
Entered Medline: 19910829

AB Monoclonal antibodies were raised against human glial **hyaluronate-binding** protein (GHAP), a major CNS-specific glycoprotein known to **bind** **hyaluronate** in vitro. Frozen sections of dog and human spinal cord were digested with Streptomyces hyaluronidase in order to ascertain whether GHAP is **bound** to **hyaluronate** in vivo. Digestion with hyaluronidase, prior to staining of the sections by conventional indirect immunofluorescence, led to a drastic reduction in the intensity of the staining reaction. Chondroitinase ABC (protease-free) was also effective in bringing about the release of GHAP from tissue sections. This enzyme also degrades **hyaluronate**. The effects of the chondroitinase were completely reversed by the addition of 1 mM Zn2+, a known inhibitor of this enzyme. The intact protein was released into the soluble fraction of human brain homogenates by testicular hyaluronidase. An immunoreactive species of 70 **kD** was released into the soluble fraction of dog spinal cord homogenates by Streptomyces hyaluronidase. Dog GHAP was isolated from spinal cord by means of ion exchange and affinity chromatography. This protein **bound** efficiently to **hyaluronate** in vitro. Dog and human GHAP had identical isoelectric points and similar peptide maps but different **molecular weights**. Dog GHAP (70 **kD**) was larger than its human counterpart (60 **kD**). These findings imply that GHAP exists in association with **hyaluronate** in CNS white matter. Immunoelectron microscopy revealed that GHAP fills the space between myelin sheaths in dog spinal cord white matter. One is led to conclude therefore that an **hyaluronate** based extracellular matrix exists in CNS white matter.

L15 ANSWER 25 OF 40 MEDLINE

ACCESSION NUMBER: 91282554 MEDLINE
DOCUMENT NUMBER: 91282554 PubMed ID: 1711835
TITLE: Oxygen derived free radicals and synovial fluid hyaluronate.

AUTHOR: Saari H
CORPORATE SOURCE: Fourth Department of Medicine, Helsinki University Central Hospital, Finland.

SOURCE: ANNALS OF THE RHEUMATIC DISEASES, (1991 Jun) 50 (6) 389-92.
Journal code: 0372355. ISSN: 0003-4967.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910818
Last Updated on STN: 19960129
Entered Medline: 19910801

AB High performance liquid chromatography with TSK 5000 PW or TSK 6000 PW size exclusion columns combined with a 125I labelled **hyaluronic** acid **binding** protein assay was used to study the effects of oxygen derived free radicals on synovial fluid **hyaluronate**. A continuous flux of free radicals was generated by the xanthine oxidase/hypoxanthine system. When the free radical flux was generated with xanthine oxidase/hypoxanthine in the presence of the iron chelator desferrioxamine and the hydroxyl radical scavenger mannitol a 30-50% decrease in **hyaluronate** peak was detected, but the **molecular weight** of synovial fluid **hyaluronate** remained almost unchanged as a result of reaction with superoxide radicals and hydrogen peroxide. When trace amounts of iron and EDTA were present in the reaction mixture depolymerisation of synovial fluid **hyaluronate** occurred, and it reached a final **molecular weight** of about 13,500 **daltons**. These results suggest that superoxide and hydroxyl radicals may have a different mode of action on synovial fluid **hyaluronate**. Superoxide radicals and hydrogen peroxide do not induce depolymerisation but, rather, change the molecular configuration of synovial fluid **hyaluronate**.

L15 ANSWER 26 OF 40 MEDLINE
ACCESSION NUMBER: 91257424 MEDLINE
DOCUMENT NUMBER: 91257424 PubMed ID: 1710584
TITLE: Characterization of a **hyaluronic** acid-**binding** protein from sheep brain comparison with human brain hyaluronectin.

AUTHOR: Delpech B; Maingonnat C; Delpech A; Maes P; Girard N; Bertrand P
CORPORATE SOURCE: Laboratoire d'Oncologie moleculaire, Centre Henri-Becquerel, Rouen, France.

SOURCE: INTERNATIONAL JOURNAL OF BIOCHEMISTRY, (1991) 23 (3) 329-37.
Journal code: 0250365. ISSN: 0020-711X.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19910802

Last Updated on STN: 19960129
Entered Medline: 19910718

AB 1. A **hyaluronic** acid (**HA**)-**binding** glycoprotein from sheep brain was characterized. 2. The specific affinity for **HA** was shown in vitro by high performance liquid chromatography, polyacrylamide gel electrophoresis and ELISA methods. 3. The **KD** for high **molecular weight HA** was 5.4 10(-9) M at 37 degrees C and lower than 10(-10) M at 4 degrees C. 4. No **link** protein was found and **HA** molecules could **bind** up to 10 times their weight of the glycoprotein. 5. The specific site for interaction was the **HA**-derived decasaccharide HA10. 6. The protein is composed of one polypeptidic chain. Tryptophan and lysine play a prominent role in the conformation of the **binding** site to **HA**. 7. Enzyme analysis indicated that the protein different forms are due to differences in glycosylation and that N- and O-**linkages** coexist in the molecules. 8. Immunohistochemistry localized the glycoprotein at the nodes of Ranvier and at the periphery of neurons. The perineuronal labeling was seen around all neurons studied in the cerebellum whereas it was almost undetectable in the cerebral hemispheres. 9. **HA** is not saturated by hyaluronectin (HN) in the sheep nervous system. 10. The glycoprotein is largely similar to human brain HN, and different from the **hyaluronate-binding** protein characterized in the cartilage.

L15 ANSWER 27 OF 40 MEDLINE
ACCESSION NUMBER: 91285236 MEDLINE
DOCUMENT NUMBER: 91285236 PubMed ID: 1711984
TITLE: Monoclonal antibody to chick embryo hyaluronan-binding protein: changes in distribution of binding protein during early brain development.
AUTHOR: Banerjee S D; Toole B P
CORPORATE SOURCE: Department of Anatomy and Cellular Biology, Tufts University Health Science Schools, Boston, Massachusetts 02111.
CONTRACT NUMBER: DE05838 (NIDCR)
HD23681 (NICHD)
SOURCE: DEVELOPMENTAL BIOLOGY, (1991 Jul) 146 (1) 186-97.
Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910825
Last Updated on STN: 20000303
Entered Medline: 19910808

AB A monoclonal antibody, MAb IVd4, that recognizes **hyaluronan -binding** protein (HABP) from chick embryo brain **has** been produced and characterized. By immunoblotting, MAb IVd4 was shown to recognize three proteins in chick embryo brain of **molecular weight** 93, 90, and 69 **kDa**; this interaction was inhibited by addition of **hyaluronan** hexasaccharides. Overlay of transblots with [3H]**hyaluronan** showed **binding** to proteins of similar **molecular weight**. MAb IVd4 blocked **binding** of [3H] **hyaluronan** to brain HABP and to simian virus-transformed 3T3

cells, indicating a possible relationship with the 85-**kDa** **hyaluronan** receptor of these cells. The distribution of HABP during early brain development was analyzed by immunohistochemistry. Immunoreactivity was uniform in newly formed neuroectoderm but became more concentrated in the roof of the brain during the second day of embryonic development. As the neuroectoderm becomes layered, the HABP was increasingly restricted to the forming plexiform layer, an area enriched in neural cell processes. Immunoreactivity was greatly enhanced by pretreatment of tissue with hyaluronidase, presumably due to removal of **hyaluronan bound** to the HABP, and was abolished on treatment with **hyaluronan** hexasaccharide, presumably due to inhibition of HABP-antibody interaction. These results suggest that a **hyaluronan** receptor is involved in early cellular events in brain development.

L15 ANSWER 28 OF 40 MEDLINE
ACCESSION NUMBER: 92192046 MEDLINE
DOCUMENT NUMBER: 92192046 PubMed ID: 1724753
TITLE: Purification, partial characterization of rat kidney **hyaluronic** acid **binding** protein and its localization on the cell surface.
AUTHOR: Gupta S; Batchu R B; Datta K
CORPORATE SOURCE: Biochemistry Laboratory, School of Environmental Sciences, Jawaharlal Nehru University, New Delhi, India.
SOURCE: EUROPEAN JOURNAL OF CELL BIOLOGY, (1991 Oct) 56 (1) 58-67.
Journal code: 7906240. ISSN: 0171-9335.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 19920509
Last Updated on STN: 19960129
Entered Medline: 19920417

AB **Hyaluronic** acid **binding** protein (HABP) **has** been purified to homogeneity from normal adult rat kidney by **hyaluronate** Sepharose affinity chromatography, and its apparent molecular mass was found to be 68 **kDa**. Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) analysis of HABP under reducing as well as nonreducing conditions revealed a single protein band of 34 **kDa**, thus indicating that kidney HABP is a homodimer and lacks interchain disulfide bond. Its glycoprotein nature was demonstrated by Con-A **binding** analysis. The pI value of kidney HABP was 6, indicating its acidic nature. Polyclonal antibodies were raised against it, and the monospecificity of the antibodies towards HABP was confirmed by Western blot analysis of tissue extracts. Immunoblot analysis **has** elucidated the occurrence of this glycoprotein in various tissues. Moreover, HABP present in these tissues are shown to be structurally and immunologically identical. However, this glycoprotein is antigenically distinct from other well characterized extracellular proteins, e.g., fibronectin, laminin and collagen type IV. With the help of enzyme-**linked** immunosorbent assay (ELISA) and iodinated [125I]HABP, it **has** been shown that kidney HABP **binds** specifically to **hyaluronic** acid (**HA**) amongst all the glycosaminoglycans (GAGs),

however, HABP can interact with other matrix proteins, e.g., laminin, fibronectin, and collagen type IV. The apparent dissociation constants of HABP for **HA**, laminin, fibronectin, and collagen type IV were approximately in the range of 10(-9) M, and kinetic analysis showed that these **binding** interactions were complex and of positive cooperative nature. Indirect immunofluorescence staining demonstrated its localization on human fetus lung fibroblast cell surface. Detection of 34 **kDa** HABP in the serum-free supernatant culture medium of fibroblasts was further evident by immunoblot analysis, thus confirming the secretory nature of HABP and its occurrence in the extracellular matrix.

L15 ANSWER 29 OF 40 MEDLINE
ACCESSION NUMBER: 91137608 MEDLINE
DOCUMENT NUMBER: 91137608 PubMed ID: 1704797
TITLE: Hyaluronan-binding proteins on cultured J 774 macrophages.
AUTHOR: Gustafson S; Forsberg N
CORPORATE SOURCE: Department of Medical and Physiological Chemistry, University of Uppsala, Sweden.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1991 Jan 10) 1091 (1) 36-40.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910412
Last Updated on STN: 19960129
Entered Medline: 19910327

AB Cultivated macrophages of murine cell-line J 774 were found to **bind** high-**molecular-weight** (**molecular weight** average approx. 5.10(6) [3H] **hyaluronan** (**HA**) by a saturable mechanism at 4 degrees C. Half-maximal **binding** was observed at 7-8 microgram/ml (1.4-1.6 nM) and the maximal **binding** was reached at 30-40 microgram/ml. Scatchard plot analysis revealed that approx. 20,000 molecules could **bind** to each cell with a **Kd** of 1.5 nM. The **binding** could be effectively inhibited by unlabeled **HA**. Also chondroitin sulphate inhibited the **binding**, but only to about 50%. At 37 degrees C the J 774 cells took up and degraded the polysaccharide effectively. Affinity chromatography on **HA coupled** to agarose of solubilized surface-iodinated J 774 cells, revealed that a protein of approx. 60 **kDa**, when analyzed by sodium dodecylsulfate polyacrylamide gel electrophoresis and autoradiography, could be specifically eluted with **HA** -oligosaccharides. Our results suggest that J 774 macrophages can **bind HA** by a mechanism compatible with receptor-**binding**, and carry a 60 **kDa HA**-**binding** protein on their surface. This receptor-**binding** may mediate uptake and degradation of the polysaccharide and influence the levels and turnover of **HA** in interstitial fluid as well as the release of **HA** into the bloodstream.

L15 ANSWER 30 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1990-193258 [25] WPIDS
DOC. NO. NON-CPI: N1990-150372
DOC. NO. CPI: C1990-083602
TITLE: Pharmaceutical prepn. for use in vivo - comprises combination of 1 or several receptor-**binding** proteins for **binding** growth factor or hormones and **hyaluronic** acid (deriv.).

DERWENT CLASS: A96 B04 P34
INVENTOR(S): NORSTEDT, G; PRISELL, P
PATENT ASSIGNEE(S): (PRIS-I) PRISELL P; (NORS-I) NORSTEDT G
COUNTRY COUNT: 32
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9005522	A	19900531	(199025)*		14
RW: AT BE CH DE FR GB IT LI NL OA SE					
W: AU BB BG BR DK ES FI HU JP KP KR LK MC MG MW NO RO SD SU US					
AU 8945253	A	19900612	(199036)		
EP 444081	A	19910904	(199136)		
R: AT BE CH DE ES FR IT LI LU NL SE					
JP 05505169	W	19930805	(199336)		9
US 5470829	A	19951128	(199602)		7
JP 2752209	B2	19980518	(199825)		4
EP 444081	B1	19990512	(199923)	EN	
R: AT BE CH DE ES FR GB IT LI LU NL SE					
DE 68928993	E	19990617	(199930)		
ES 2134187	T3	19991001	(199948)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 444081	A		EP 1989-912690	19891117
JP 05505169	W		JP 1989-511728	19891117
			WO 1989-SE666	19891117
US 5470829	A	CIP of	US 1991-690898	19910622
			US 1993-37124	19930325
JP 2752209	B2		JP 1989-511728	19891117
			WO 1989-SE666	19891117
EP 444081	B1		EP 1989-912690	19891117
			WO 1989-SE666	19891117
DE 68928993	E		DE 1989-628993	19891117
			EP 1989-912690	19891117
			WO 1989-SE666	19891117
ES 2134187	T3		EP 1989-912690	19891117

FILING DETAILS:

PATENT NO	KIND		PATENT NO
JP 05505169	W	Based on	WO 9005522
JP 2752209	B2	Previous Publ.	JP 05505169
		Based on	WO 9005522
EP 444081	B1	Based on	WO 9005522
DE 68928993	E	Based on	EP 444081

Based on WO 9005522
ES 2134187 T3 Based on EP 444081

PRIORITY APPLN. INFO: SE 1988-4164 19881117
AN 1990-193258 [25] WPIDS
AB WO 9005522 A UPAB: 19930928
A pharmaceutical prepn for use in vivo comprises a combination of one or several receptor/**binding** proteins for **binding** growth factors or hormones and **hyaluronic** acid or its derivs or a biodegradable polymer, opt in combination with its/their ligands to achieve slow release of growth factors and hormones.

The receptors **binding** proteins are mixed with or **covalently bound** to **hyaluronic** acid or the biodegradable polymer. The receptor **binding** proteins are insulin growth factor-1-receptor, insulin growth factor-2-receptors, insulin receptor, platelet derived growth factor receptor, Fibroblast growth factor receptor, Epidermal growth factor receptor, nerve growth factor etc.

The biodegradable polymers are polyglycolide (PGA), Copolymers of glycolide, glycolide/L-lactide copolymers (PGA/PLLA), glycolide/trimethylene carbonate copolymers polylactides, (PLA) Stereocopolymers of PLA Poly-L-lactide (PLLA) etc.

The ligand are insulin growth factor-1 and 2; (1GF-1, 1GF-2) platelet derived growth factor (PDGF), Epidermal growth factor (EGF), Fibroblast growth factor (FGF), nerve growth factor (NGF) etc.

USE/ADVANTAGE - The principles according to the invention may be useful in the situation of abnormal, increased prodcn of growth factors, eg tumour growth, the **carrier** + receptor/**binding protein** acting as a selective resorption agent of growth factors.

0/0

ABEQ JP 05505169 W UPAB: 19931122
A pharmaceutical prepn. for use in vivo comprises a combination of one or several receptor/**binding** proteins for **binding** growth factors or hormones and **hyaluronic** acid or its derivs. or a biodegradable polymer, opt. in combination with its/their ligands to achieve slow release of growth factors and hormones.

The receptors **binding** proteins are mixed with or **covalently bound** to **hyaluronic** acid or the biodegradable polymer. The receptor **binding** proteins are insulin growth factor-1 receptor, insulin growth factor-2 receptors, insulin receptor, platelet derived growth factor receptor. Fibroblast growth factor receptor, Epidermal growth factor receptor, nerve growth factor, etc..

The biodegradable polymers are polyglycolide (PGA), copolymers of glycolide, glycolide/L-lactide copolymers (PGA/PLLA), glycolide/trimethylene carbonate copolymers polylactides, (PLA) Stereocopolymers of PLA Poly-L-lactide (PLLA), etc..

The ligand are insulin growth factor-1 and -2; (1GF-1, 1GF-2) platelet derived growth factor (PDGF), Epidermal growth factor (EGF), Fibroblast growth factor (FGF), nerve growth factor (NGF), etc..

USE/ADVANTAGE - The principles according to the invention may be useful in the situation of abnormal, increased prodn. of growth factors, e.g., tumour growth, the **carrier** and receptor/

binding protein acting as a selective resorption agent of growth factors.

ABEQ US 5470829 A UPAB: 19960115

In a method for administering ligand selected from the group consisting of growth factors and hormones to an animal comprising administering said ligand in combination with an adjuvant which controls the release of said ligand, said adjuvant comprising a biodegradable polymer and a receptor for said ligand, wherein said receptor is **conjugated** to a biodegradable polymer, the improvement wherein

said receptor comprises (1) a protein for **binding** said ligand, said protein being selected from the group consisting of insulin-like growth factor-1-receptor; erythropoietin-receptor; insulin-like growth factor-2-receptor; insulin-receptor; platelet derived growth factor-receptor; fibroblast growth factor-receptor; colony stimulating growth factor-receptor; transforming growth factor-receptor; growth hormone-receptor; parathyroid hormone-receptor; calcitonin-receptor; estrogen-receptor; insulin-like growth factor serum **binding** protein; epidermal growth factor receptor; corticosteroid **binding** globulin; and bone morphogenic protein and

(2) said biodegradable polymer is selected from the group consisting of alginates; **hyaluronic** acid and derivatives thereof: polyglycolide; copolymers of glycolide; copolymers of glycolide and L-lactide; copolymers of glycolide and trimethylene carbonate; polylactides; stereo-copolymers of polylactides; poly-L-lactide; poly-DL-lactide; copolymers of L-lactide and DL-lactide; copolymers of polylactide; copolymers of lactide and tetramethylglycolide; copolymers of lactide and trimethylene carbonate; copolymers of lactide and alpha-valerolactone; copolymers of lactide and epsilon-caprolactone; copolymers of polylactide and polyethylene oxide; copolymers of poly-beta-hydroxybutyrate; polyurethanes; methylmethacrylate-N-vinyl pyrrolidone copolymers; and poly-p-dioxanone;

said ligand being a ligand specific to said protein and being **linked** to said protein.

Dwg.0/0

L15 ANSWER 31 OF 40 MEDLINE

ACCESSION NUMBER: 90203016 MEDLINE
DOCUMENT NUMBER: 90203016 PubMed ID: 1690737
TITLE: **Hyaluronic** acid associated with the surfaces of cultured fibroblasts is **linked** to a serum-derived 85-**kDa** protein.
AUTHOR: Yoneda M; Suzuki S; Kimata K
CORPORATE SOURCE: Institute of Molecular Science of Medicine, Aichi Medical University, Japan.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1990 Mar 25) 265 (9) 5247-57.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19960129
Entered Medline: 19900502

AB **Hyaluronic** acid (**HA**) was extracted from the cell layer of cultured mouse dermal fibroblasts with 6 M guanidine HCl in the presence of 8% (w/v) Zwittergent. **HA** could be separated from the bulk of extracted proteins by consecutive isopycnic centrifugation and gel and ion-exchange chromatography under dissociative conditions. The final preparation was the complex of **HA** (viscosity average **molecular weight** approximately 2 x 10(6)) and a protein of Mr approximately 85,000 in a molar ratio of 1:1. Since the extraction procedure employed **has** been shown to break most noncovalent bonds between **HA** and proteins, they would appear to be **covalently linked**. However, the **HA-binding** protein remained unlabeled even after long incubation of the cells in the presence of a highly radioactive amino acid mixture, suggesting that it is an exogenous protein derived from the fetal calf serum added to culture medium. The presence of a **HA-binding** 85-**kDa** protein could in fact be demonstrated in fetal calf serum as well as sera from various other sources. This protein cross-reacted with antibodies raised against the **HA**-protein complex purified from cultured mouse dermal cells and was retained on octyl-Sepharose. Like the cell-derived 85-**kDa** protein, the serum 85-**kDa** protein, once **bound** to **HA** , could not be released from the complex by various dissociative procedures. These results, taken together, suggest that the hydrophobic serum protein can be intercalated into cell surface membranes, thereby mediating the **binding** of **HA** to the cell surface.

L15 ANSWER 32 OF 40 MEDLINE

ACCESSION NUMBER:	90079444 MEDLINE
DOCUMENT NUMBER:	90079444 PubMed ID: 1688375
TITLE:	**Hyaluronate-binding** proteins of murine brain.
AUTHOR:	Marks M S; Chi-Rosso G; Toole B P
CORPORATE SOURCE:	Department of Anatomy and Cellular Biology, Tufts University Health Sciences Center, Boston, Massachusetts 02111.
CONTRACT NUMBER:	DE05838 (NIDCR)
SOURCE:	JOURNAL OF NEUROCHEMISTRY, (1990 Jan) 54 (1) 171-80. Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY:	United States
	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199001
ENTRY DATE:	Entered STN: 19900328
	Last Updated on STN: 20000303
	Entered Medline: 19900119

AB The distribution of **hyaluronate-binding** activity was determined in the soluble and membrane fractions derived from adult mouse brain by sonication in low-ionic-strength buffer. Approximately 60% of the total activity was recovered in the soluble fraction and 33% in membrane fractions. In both cases, the **hyaluronate-binding** activities were found to be of high affinity (**KD** = 10(-9) M), specific for **hyaluronate**, and glycoprotein in nature. Most of the **hyaluronate-binding** activity from the soluble

fraction chromatographed in the void volume of Sepharose CL-4B and CL-6B. Approximately 50% of this activity was highly negatively charged, eluting from diethylaminoethyl (DEAE)-cellulose in 0.5 M NaCl, and contained chondroitin sulfate chains. This latter material also reacted with antibodies raised against cartilage **link** protein and the core protein of cartilage proteoglycan. Thus, the **binding** and physical characteristics of this **hyaluronate-binding** activity are consistent with those of a chondroitin sulfate proteoglycan aggregate similar to that found in cartilage. A 500-fold purification of this proteoglycan-like, **hyaluronate-binding** material was achieved by wheat germ agglutinin affinity chromatography, molecular sieve chromatography on Sepharose CL-6B, and ion exchange chromatography on DEAE-cellulose. Another class of **hyaluronate-binding** material (25-50% of that recovered) eluted from DEAE with 0.24 M NaCl; this material had the properties of a complex glycoprotein, did not contain chondroitin sulfate, and did not react with the antibodies against cartilage **link** protein and proteoglycan. Thus, adult mouse brain contains at least three different forms of **hyaluronate-binding** macromolecules. Two of these have properties similar to the **link** protein and proteoglycan of cartilage proteoglycan aggregates; the third is distinguishable from these entities.

L15 ANSWER 33 OF 40 MEDLINE
ACCESSION NUMBER: 89380477 MEDLINE
DOCUMENT NUMBER: 89380477 PubMed ID: 2476451
TITLE: Membrane-associated **hyaluronate-binding** activity of chondrosarcoma chondrocytes.
AUTHOR: McCarthy M T; Toole B P
CORPORATE SOURCE: Department of Anatomy and Cellular Biology, Tufts University Health Sciences Center, Boston, Massachusetts 02111.
CONTRACT NUMBER: DE05838 (NIDCR)
SOURCE: JOURNAL OF CELLULAR PHYSIOLOGY, (1989 Oct) 141 (1) 191-202.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19990129
Entered Medline: 19891025

AB The association of **hyaluronate** with the surface of chondrocytes was examined by several approaches using primary cultures of chondrocytes derived from the Swarm rat chondrosarcoma. In culture, chondrosarcoma chondrocytes produced large pericellular coats, which can be visualized by particle exclusion, and which can be removed by Streptomyces hyaluronidase. Exposure of chondrocytes, which had been metabolically labelled with 3H-acetate, to exogenous **hyaluronate** or to Streptomyces hyaluronidase resulted in the release of 36-38% of the endogenous, labelled chondroitin sulfate from the cell layer into the incubation solution. These results imply that at least 37% of the cell layer chondroitin sulfate

proteoglycan is retained there by an interaction with **hyaluronate**. Thus membranes were prepared from cultured chondrocytes and examined for sites which **bind** 3H-**hyaluronate**. **Binding** was observed and found to be saturable, specific for **hyaluronate**, of high affinity (**Kd** = approximately 10(-10) M), and destroyed by treating the membranes with trypsin. The 3H-**hyaluronate-binding** activity was inhibited competitively by **hyaluronate** decasaccharides but not by hexasaccharides or octasaccharides, indicating that the **binding** sites recognize a sequence of **hyaluronate** composed of five disaccharide repeats. The **binding** activity was partially purified from a detergent extract of chondrocyte membranes by ion exchange chromatography on DEAE-cellulose, followed by affinity chromatography on wheat germ agglutinin-agarose. Analysis of the partially purified **binding** activity by SDS-PAGE revealed five protein bands of 48,000-66,000 **daltons** in silver-stained gels. SDS-PAGE followed by Western blotting and exposure to monoclonal antibodies which recognize epitopes present in **link** protein and in the **hyaluronate-binding** region of cartilage proteoglycan revealed no immunoreactive protein bands in the partially purified material. We conclude that one mechanism by which **hyaluronate** associates with the chondrocyte surface may be via interaction with a membrane-**bound hyaluronate** **-binding** protein which is distinct from **link** protein and proteoglycan.

L15 ANSWER 34 OF 40 MEDLINE

ACCESSION NUMBER: 89229983 MEDLINE
DOCUMENT NUMBER: 89229983 PubMed ID: 2469524
TITLE: Structural similarity of **hyaluronate** **binding** proteins in brain and cartilage.
AUTHOR: Bignami A; Lane W S; Andrews D; Dahl D
CORPORATE SOURCE: Department of Pathology, Harvard Medical School, West Roxbury, MA 02132.
CONTRACT NUMBER: NS 13034 (NINDS)
SOURCE: BRAIN RESEARCH BULLETIN, (1989 Jan) 22 (1) 67-70. Journal code: 7605818. ISSN: 0361-9230.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19890612

AB A glial **hyaluronate-binding** protein (GHAP) was isolated from human brain white matter by affinity chromatography on immobilized **hyaluronate**. The 60 **kDa** protein appeared remarkably homogeneous by reversed-phase high pressure liquid chromatography analysis. Four cyanogen bromide peptides and 10 tryptic peptides were characterized by amino acid sequence, a total of 12 sequences since overlaps were found between 2 cyanogen bromide and 2 tryptic peptide sequences. Two sequences of brain GHAP had similarity with rat **link** protein, a **hyaluronate binding** protein in cartilage. The region of similarity was contained in the evolutionary conserved COOH-terminal half of **link** protein which is involved in

the **binding** of **hyaluronate**. The remaining 10 amino acid sequences of brain GHAP had no similarity with **link** protein, nor with previously reported protein sequences. The findings suggest that the **hyaluronate** **binding** domains of such diverse proteins as brain GHAP and cartilage **link** protein are similar, probably due to the fact that **hyaluronic** acid is highly conserved in evolution.

L15 ANSWER 35 OF 40 MEDLINE
ACCESSION NUMBER: 88256297 MEDLINE
DOCUMENT NUMBER: 88256297 PubMed ID: 3290104
TITLE: Heparin-inhibitable basement membrane-binding protein of Streptococcus pyogenes.
AUTHOR: Bergey E J; Stinson M W
CORPORATE SOURCE: Department of Microbiology, School of Medicine and Biomedical Sciences, State University of New York, Buffalo 14214.
CONTRACT NUMBER: RO1-DE05696 (NIDCR)
SOURCE: INFECTION AND IMMUNITY, (1988 Jul) 56 (7) 1715-21. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198808
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880801

AB Solubilized surface proteins of Streptococcus pyogenes serotype M6 were found by indirect immunofluorescence assays to **bind** selectively to proteoglycan-containing regions of basement membranes of kidney and cardiac muscle in vitro. Epithelial, endothelial, and interstitial cells were unstained. **Binding** of streptococcal protein to basement membranes was competitively inhibited by heparin and, to a lesser extent, by heparan sulfate. Weak inhibition was also observed with other glycosaminoglycans, including dermatan sulfate, chondroitin sulfate, and **hyaluronic** acid. Type IV collagen, gelatin, serum fibronectin, **glucuronic** acid, and a selection of monosaccharides had no significant effects on **binding**. The heparin-inhibitable basement membrane-**binding** protein was purified by affinity chromatography on heparin-Sepharose 6-B. Polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate and urea dissociated the affinity-purified protein into two polypeptides of 9,000 and 15,000 mrs. Chemical analyses revealed that the purified protein was devoid of cysteine, amino and neutral sugars, and phosphate. Thus, the polypeptides are not glycosylated or complexed with trace amounts of lipoteichoic acid or polysaccharide. **Binding** of purified protein to tissue was determined by direct radioassay and indirect immunofluorescence and was inhibitable by heparin. Although the in vivo effects of this streptococcal component remain to be determined, its deposition on basement membranes in vitro supports the hypothesis that it contributes to the pathogenesis of poststreptococcal glomerulonephritis or acute rheumatic fever.

L15 ANSWER 36 OF 40 MEDLINE

ACCESSION NUMBER: 87271596 MEDLINE
DOCUMENT NUMBER: 87271596 PubMed ID: 2440472
TITLE: Characterization of **hyaluronate** **binding** proteins isolated from 3T3 and murine sarcoma virus transformed 3T3 cells.

AUTHOR: Turley E A; Moore D; Hayden L J
SOURCE: BIOCHEMISTRY, (1987 Jun 2) 26 (11) 2997-3005.
Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198709
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19870923

AB A **hyaluronic** acid **binding** fraction was purified from the supernatant media of both 3T3 and murine sarcoma virus (MSV) transformed 3T3 cultures by **hyaluronate** and immunoaffinity chromatography. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis resolved the **hyaluronate** affinity-purified fraction into three major protein bands of estimated **molecular weight** (Mr,e) 70K, 66K, and 56K which contained **hyaluronate binding** activity and which were termed **hyaluronate binding** proteins (HABP). **Hyaluronate** affinity chromatography combined with immunoaffinity chromatography, using antibody directed against the larger HABP, allowed a 20-fold purification of HABP. Fractions isolated from 3T3 supernatant medium also contained additional **binding** molecules in the **molecular** **weight** range of 20K. This material was present in vanishingly small amounts and was not detected with a silver stain or with [35S]methionine label. The three protein species isolated by **hyaluronate** affinity chromatography (Mr,e 70K, 66K, and 56K) were related to one another since they shared antigenic determinants and exhibited similar pI values. In isocratic conditions, HABP occurred as aggregates of up to 580 **kilodaltons**. Their glycoprotein nature was indicated by their incorporation of 3H-sugars. Enzyme-**linked** immunoadsorbent assay showed they were antigenically distinct from other **hyaluronate** **binding** proteins such as fibronectin, cartilage **link** protein, and the **hyaluronate binding** region of chondroitin sulfate proteoglycan. The apparent dissociation constant of HABP for **hyaluronate** was approximately 10(-8) M, and kinetic analyses showed these **binding** interactions were complex and of a positive cooperative nature.(ABSTRACT TRUNCATED AT 250 WORDS)

L15 ANSWER 37 OF 40 MEDLINE
ACCESSION NUMBER: 86323228 MEDLINE
DOCUMENT NUMBER: 86323228 PubMed ID: 2428366
TITLE: Studies on the affinity of **hyaluronic** acid **binding** protein to glycosaminoglycans.

AUTHOR: D'Souza M; Datta K
SOURCE: BIOCHEMISTRY INTERNATIONAL, (1986 Jul) 13 (1) 89-100.
Journal code: 8100311. ISSN: 0158-5231.

PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198610
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19861015

AB The affinity of **hyaluronic** acid **binding** protein (HBP) to different glycosaminoglycans (GAGs) was examined. The purified protein was pretreated with **hyaluronic** acid (**HA**), heparin, **glucuronic** acid and N-Acetyl-glucosamine and was loaded onto **Hyaluronate** -Sepharose affinity column. The **binding** of HBP to **HA** immobilized on sepharose column was specifically blocked only by pretreatment of HBP to **HA** and the elution of HBP was decreased proportionately with the addition of higher quantity of HBP. The specificity of HBP to **HA** was confirmed as it did not **bind** to Heparin-Sepharose or Chondroitin-4-Sulphate-Sepharose columns. The complex of HBP in association with **HA** was further shown on Sephadex G-200 and 7.5% polyacrylamide gel. All the experimental findings indicate that HBP **binds** specifically to **HA** only.

L15 ANSWER 38 OF 40 MEDLINE
ACCESSION NUMBER: 86323227 MEDLINE
DOCUMENT NUMBER: 86323227 PubMed ID: 2428365
TITLE: A novel glycoprotein that **binds** to **hyaluronic** acid.
AUTHOR: D'Souza M; Datta K
SOURCE: BIOCHEMISTRY INTERNATIONAL, (1986 Jul) 13 (1) 79-88.
Journal code: 8100311. ISSN: 0158-5231.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198610
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19861015

AB **Hyaluronic** acid **binding** protein (HBP) **has** been purified to homogeneity from normal rat brain by using **Hyaluronate**-Sepharose affinity chromatography. It appears as a single band in non-dissociating gel electrophoresis. The **molecular weight** of native protein, as determined by gel filtration is found to be 68,000 **daltons** , and **has** a single subunit of **molecular weight** approximately 13,500 as determined under denaturing conditions in polyacrylamide gel electrophoresis, indicating that this protein is apparently composed of five identical subunits. Amino acid analysis shows the purified HBP to be rich in glycine and glutamic acid content, and is distinct from fibronectin, **link** proteins, and gelatin **binding** proteins which are known to **bind** to **hyaluronic** acid. This protein is further characterised as sialic acid containing glycoprotein.

L15 ANSWER 39 OF 40 MEDLINE
ACCESSION NUMBER: 85174504 MEDLINE
DOCUMENT NUMBER: 85174504 PubMed ID: 2580533

TITLE: Evidence for naturally occurring **hyaluronic** acid **binding** protein in rat liver.
AUTHOR: D'Souza M; Datta K
SOURCE: BIOCHEMISTRY INTERNATIONAL, (1985 Jan) 10 (1) 43-51. Journal code: 8100311. ISSN: 0158-5231.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198505
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850515

AB **Hyaluronic** acid **binding** protein (HBP) was purified homogeneously from normal adult rat liver by **hyaluronate**-sepharose affinity chromatography. The **molecular weight** of this protein as determined by gel filtration was found to be 64,000 **daltons**. This protein HBP appeared as a single band in non-dissociating gel electrophoresis and **has** a subunit of **molecular weight** approximately 12,000 as determined by SDS-gel electrophoresis.

L15 ANSWER 40 OF 40 MEDLINE
ACCESSION NUMBER: 82097235 MEDLINE
DOCUMENT NUMBER: 82097235 PubMed ID: 7033140
TITLE: Isolation of heart- and kidney-**binding** protein from **group A streptococci**.
AUTHOR: Stinson M W; Bergey E J
CONTRACT NUMBER: N01-DE-72408 (NIDCR)
R01-DE-05696 (NIDCR)
SOURCE: INFECTION AND IMMUNITY, (1982 Jan) 35 (1) 335-42. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198203
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 20000303
Entered Medline: 19820322

AB Tritium-labeled, water-soluble components of Streptococcus pyogenes type M6 absorbed to cardiac tissue in vitro. Tissue binding was time dependent, saturable, and reversible. Chromatography of the crude bacterial extract on Bio-Gel P-300 indicated a **molecular weight** greater than 300,000 for the heart-binding component. Sodium dodecyl sulfate (SDS) dissociated this aggregate into a protein of 18,000 to 20,000 **daltons** as determined by Sephacryl S-200 chromatography and SDS-polyacrylamide disc gel electrophoresis. The tissue-binding protein was also purified from streptococcal extracts by absorption to immobilized heart components. SDS-polyacrylamide gel electrophoresis of the protein desorbed from tissue revealed a radioactive band of 19,000 **daltons**. Indirect immunofluorescence tests on cardiac tissue treated with streptococcal extract showed an accumulation of a bacterial antigen on the sarcolemmal sheaths. Streptococcal components also adsorbed to basement membranes of kidney. Antisera

prepared to isolated cytoplasmic membranes and water-soluble extracts of S. pyogenes type M6 were the most sensitive reagents for the detection of bacterial components bound to tissue. Antisera prepared to isolated cell walls and to intact bacteria were weakly reactive in these assays.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, TOXCENTER, PHIC, PHIN' ENTERED AT 15:47:24 ON 27 JUN 2002)

Author (8)

L16 339 SEA ABB=ON PLU=ON MICHON F?/AU
L17 6389 SEA ABB=ON PLU=ON MOORE S?/AU
L18 1381 SEA ABB=ON PLU=ON BLAKE M?/AU
L19 1144 SEA ABB=ON PLU=ON (LAUDE SHARP M? OR SHARP LAUDE M? OR LAUDE M? OR SHARP M?)/AU

L20 3 SEA ABB=ON PLU=ON L16 AND L17 AND L18 AND L19
L21 52 SEA ABB=ON PLU=ON L16 AND (L17 OR L18 OR L19)
L22 5 SEA ABB=ON PLU=ON L17 AND (L18 OR L19)
L23 12 SEA ABB=ON PLU=ON L18 AND L19
L24 23 SEA ABB=ON PLU=ON (L21 OR L16 OR L17 OR L18 OR L19) AND L7
L25 37 SEA ABB=ON PLU=ON L20 OR L22 OR L23 OR L24
L26 16 DUP REM L25 (21 DUPLICATES REMOVED)

L26 ANSWER 1 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 1

ACCESSION NUMBER: 2002:189021 BIOSIS
DOCUMENT NUMBER: PREV200200189021
TITLE: SpeB is inhibited by hyaluronic acid.
AUTHOR(S): Long-Rowe, K. O. (1); **Blake, M. S. (1)**
CORPORATE SOURCE: (1) Baxter Healthcare Corporation, Deerfield, IL USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 144. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001
ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Streptococcal Pyrogenic Exotoxin B (SpeB) **has** been found to be an important virulence factor of **Group A streptococcal** infections. This cysteine protease is secreted from the bacterium as an inactive 44 Kd precursor molecule which then transforms into a 32 Kd active enzyme by autolysis or exposure to reducing agents. We found that by applying the precursor of SpeB on Heparin and SP Sepharose columns that the purified active form could be recovered without addition of reducing agents or trypsin. The finding that SpeB interacted with heparin lead us to studying other glycosaminoglycans and how these polysaccharides might influence the proteolytic activity of this cysteine protease. Upon incubating purified SpeB with free heparin between 50-800 ug/ml, the enzymatic activity was reduced slightly in a non-dose dependent manner. Similar inhibition was observed using chondroitan sulfate at 600-800 ug/ml. Surprisingly, we observed that the addition of high molecular weight **hyaluronic** acid (>200,000 MW) could largely inhibit the SpeB activity in a dose dependent manner between 50-800 ug/ml. Supplemental investigations into this phenomenon of enzyme inhibition by this non-sulfated glycosaminoglycan when

compared to dextran (188,000 MW) or dextran sulfate (500,000 MW) indicated that dextran was non-inhibitory to proteolytic activity and dextran sulfate was slightly inhibitory in a non-dose dependent manner. It is speculated that the **hyaluronic** acid capsule on the streptococcus surface may protect the organism from its own activated protease. We are currently conducting experiments to determine the type of inhibition incurred on SpeB by **hyaluronic** acid and to test for the reversibility of the interaction. Although it is unusual to find such inhibitory interactions between a protease and polysaccharides, this **has** been previously observed with the Plasma **Hyaluronan-Binding** Protein which is a serine protease.

L26 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:144761 HCAPLUS
DOCUMENT NUMBER: 132:193251
TITLE: Immunogenic .beta.-propionamido-linked polysaccharide protein conjugate useful as a vaccine produced using an N-acryloylated polysaccharide
INVENTOR(S): **Michon, Francis**; Huang, Chun-Hsien; Uitz, Catherine
PATENT ASSIGNEE(S): North American Vaccine, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010599	A2	20000302	WO 1999-US18982	19990818
WO 2000010599	A3	20000622		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9957800	A1	20000314	AU 1999-57800	19990818
EP 1109576	A2	20010627	EP 1999-945115	19990818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
NO 2001000805	A	20010403	NO 2001-805	20010216

PRIORITY APPLN. INFO.:
US 1998-97120P P 19980819
US 1999-376911 A 19990818
WO 1999-US18982 W 19990818

AB Novel immunogenic .beta.-propionamido-linked polysaccharide- and N-propionamido-linked oligosaccharide-protein conjugates are provided as well as method of producing the conjugates. The conjugation procedure is simple, rapid, reproducible and applicable to a variety of polysaccharides or oligosaccharides derived from bacterial species, yeast, cancer cells or chem. synthesized.

Vaccines and methods of immunization against infection or cancer using the immunogenic .beta.-propionamido-linked polysaccharide- and .beta.-propionamido-linked oligosaccharide-protein conjugates are also disclosed.

L26 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:77590 HCAPLUS
DOCUMENT NUMBER: 130:152551
TITLE: Modified immunogenic pneumolysin compositions as vaccines
INVENTOR(S): Minetti, Conceicao; **Michon, Francis;** Pullen, Jeffrey K.; Polvino-Bodnar, Maryellen; Liang, Shu-Mei; Tai, Joseph Y.
PATENT ASSIGNEE(S): North American Vaccine, Inc., USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9903884	A2	19990128	WO 1998-US14716	19980721
WO 9903884	A3	19990408		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9884078	A1	19990210	AU 1998-84078	19980721
AU 740956	B2	20011115		
EP 998557	A2	20000510	EP 1998-934590	19980721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001510031	T2	20010731	JP 2000-503106	19980721
US 2001014332	A1	20010816	US 1998-120044	19980721
NO 2000000257	A	20000321	NO 2000-257	20000119
PRIORITY APPLN. INFO.:			US 1997-53306P P	19970721
			US 1998-73456P P	19980202
			WO 1998-US14716 W	19980721

AB This invention relates to modified pneumolysin polypeptides that retain the immunogenic nature of pneumolysin but have reduced or undetectable hemolytic activity compared to native pneumolysin. The invention also provides a method for generating novel pneumolysin variants with these desired characteristic properties. The invention also provides immunogenic compns. useful as pharmaceutical compns. including vaccines in which non-toxic, modified pneumolysin is used to stimulate protective immunity against Streptococcus pneumoniae. The vaccines may be compns. in which the modified pneumolysin in conjugated to bacterial polysaccharides or may be carried on an attenuated viral vector. In addn., the invention also provides a method of using the non-toxic, modified pneumolysin toxoid in order to stimulate antibodies against Streptococcus

pneumoniae in a treated individual which are then isolated and transferred to a second individual, thereby conferring protection against Streptococcus pneumoniae in the second individual. Prepd. and tested for immunogenicity were polypeptides pNVJ1, pNVJ20, pNVJ22, pNVJ45, pNVJ56, pNVJ103, pNVJ207, pNVJ111, and pNVJ211 and corresponding nucleic acid sequences.

L26 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 1998:707259 HCAPLUS
DOCUMENT NUMBER: 130:108851
TITLE: Preclinical studies on a recombinant group B meningococcal porin as a carrier for a novel Haemophilus influenzae type b conjugate vaccine
AUTHOR(S): Fusco, Peter C.; Michon, Francis; **Laude-Sharp, Maryline**; Minetti, Conceicao A. S. A.; Huang, Chun-Hsien; Heron, Iver; **Blake, M. S.**
CORPORATE SOURCE: North American Vaccine, Inc., Beltsville, MD, 20705, USA
SOURCE: Vaccine (1998), 16(19), 1842-1849
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In anticipation of future combination vaccines, a recombinant class 3 porin (rPorB) of group B meningococci was evaluated as an alternative carrier protein for a Haemophilus influenzae type b (Hib) polyribosylribotol phosphate (PRP) conjugate vaccine. The use of rPorB may avoid undesirable immunol. interactions among vaccine components, including epitopic suppression from conventional carriers (e.g. tetanus toxoid [TT]), as well as provide desirable immunomodulatory effects. Rats were found to be more reliable and consistent than mice or guinea pigs for studying antibody responses to the Hib conjugates. Different Hib conjugates, Hib-TT and Hib-rPorB, consisting of PRP conjugated by reductive amination to TT or rPorB, were compared in rats. Com. available, licensed vaccines, HbOC (HibTITER.RTM.) and PRP-T (OmniHib.RTM.), were used as ref. controls. Maximum geometric mean ELISA IgG titers were obtained in rats after only two doses, showing booster effects for all. However, Hib-rPorB immunization consistently resulted in responses that were 1-2 orders of magnitude greater than those for the other conjugates, including the licensed control vaccines. A max. 4600-fold rise was obsd. for Hib-rPorB after two doses, and, unlike the other conjugates, a 100% response rate was always achieved without adjuvant. These results warrant further investigation of Hib-rPorB in combination with DTaP.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 1998:644179 HCAPLUS
DOCUMENT NUMBER: 130:64887
TITLE: Multivalent pneumococcal capsular polysaccharide conjugate vaccines employing genetically detoxified pneumolysin as a carrier protein
AUTHOR(S): **Michon, Francis**; Fusco, Peter C.; Minetti, Conceicao A. S. A.; **Laude-Sharp,**

Maryline; Uitz, Catherine; Huang, Chun-Hsien; D'Ambra, Anello J.; **Moore, Samuel**; Remeta, David P.; Heron, Iver; **Blake, M. S.**
CORPORATE SOURCE: North American Vaccine, Inc., Beltsville, MD, 21046, USA
SOURCE: Vaccine (1998), 16(18), 1732-1741
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A genetically detoxified pneumolysin, pneumolysoid (PLD), was investigated as a carrier protein for pneumococcal capsular polysaccharide (CPS). Such a CPS-PLD conjugate might provide addnl. protection against pneumococcal infections and resultant tissue damage. A single point mutant of pneumolysin was selected, which lacked measurable hemolytic activity, but exhibited the overall structural and immunol. properties of the wild type. PLD conjugates were prepd. from CPS serotypes 6B, 14, 19F, and 23F by reductive amination. The structural features of free PLD, as well as the corresponding CPS-PLD, as assessed by CD spectroscopy, were virtually indistinguishable from the wild type counterpart. Each of the CPS monovalent and tetravalent conjugate formulations were examd. for immunogenicity in mice at both 0.5 and 2.0 .mu.g CPS per dose. Tetanus toxoid (TT) conjugates were similarly created and used for comparison. The resultant conjugate vaccines elicited high levels of CPS-specific IgG that was opsonophagocytic for all serotypes tested. Opsonophagocytic titers, expressed as reciprocal dilns. resulting in 50% killing using HL-60 cells, ranged from 100 to 30000, depending on the serotype and formulation. In general, the lower dose and tetravalent formulations yielded the best responses for all serotypes (i.e., either equiv. or better than the higher dose and monovalent formulations). The PLD conjugates were also generally equiv. to or better in CPS-specific responses than the TT conjugates. In particular, both the PLD conjugate and the tetravalent formulations induced responses for type 23F CPS that were approx. an order of magnitude greater than that of the corresponding TT conjugate and monovalent formulations. In addn., all the PLD conjugates elicited high levels of pneumolysin-specific IgG which were shown to neutralize pneumolysin-induced hemolytic activity in vitro. As a result of these findings, PLD appears to provide an advantageous alternative to conventional carrier proteins for pneumococcal multivalent CPS conjugate vaccines.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:249154 BIOSIS
DOCUMENT NUMBER: PREV199900249154
TITLE: Tetravalent combination conjugate vaccines against group B streptococci.
AUTHOR(S): **Laude-Sharp, M. (1)**; Fusco, P. C. (1); Uitz, C. (1); Rathmann, J. B. (1); Walker, M. S. (1); **Blake, M. S. (1)**; Michon, F. (1)
CORPORATE SOURCE: (1) North American Vaccine, Inc., Beltsville, MD USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1998) Vol.

38, pp. 301.
Meeting Info.: 38th Interscience Conference on Antimicrobial Agents and Chemotherapy San Diego, California, USA September 24-27, 1998 American Society for Microbiology

DOCUMENT TYPE: Conference
LANGUAGE: English

L26 ANSWER 7 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:249155 BIOSIS
DOCUMENT NUMBER: PREV199900249155
TITLE: Recombinant group B meningococcal porin as a carrier protein for a novel Haemophilus influenzae type B conjugate vaccine.
AUTHOR(S): Fusco, P. C. (1); Michon, F. (1); **Laude-Sharp, M. (1)**; Minetti, C.A.S.A. (1); Huang, C. H. (1); Heron, I. (1); **Blake, M. S. (1)**
CORPORATE SOURCE: (1) North American Vaccine, Inc., Beltsville, MD USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1998) Vol. 38, pp. 301.
Meeting Info.: 38th Interscience Conference on Antimicrobial Agents and Chemotherapy San Diego, California, USA September 24-27, 1998 American Society for Microbiology

DOCUMENT TYPE: Conference
LANGUAGE: English

L26 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:3733 HCAPLUS
DOCUMENT NUMBER: 128:74069
TITLE: Phagocytic, serological, and protective properties of streptococcal group A carbohydrate antibodies
AUTHOR(S): Zabriskie, J. B.; Poon-King, T.; **Blake, M. S.**; **Michon, F.**; Yoshinaga, M.
CORPORATE SOURCE: Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Advances in Experimental Medicine and Biology (1997), 418(Streptococci and the Host), 917-919
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sera from rabbits immunized with **group A streptococcal** carbohydrate (**group A coupled** with tetanus toxoid) were opsonic for a group A type 6 strain. Similar results were obtained with 3 other different M types. ELISA titers of less than 100,000 were non-phagocytic. The rabbit sera described above were able to protect mice challenged i.p. with group A streptococcal strains of 2 different M types. Thus, group A streptococcal antibodies promote phagocytosis of several different strains of A streptococci, and these antibodies passively protect against an in vivo mouse challenge model.

L26 ANSWER 9 OF 16 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97472826 MEDLINE

DOCUMENT NUMBER: 97472826 PubMed ID: 9331785
TITLE: Combination conjugate vaccines against multiple serotypes of group B streptococci.
AUTHOR: Michon F; Fusco P C; D'Ambra A J; **Laude-Sharp M**; Long-Rowe K; **Blake M S**; Tai J Y
CORPORATE SOURCE: North American Vaccine, Inc., Beltsville, Maryland, USA.
SOURCE: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1997) 418 847-50.
Journal code: 0121103. ISSN: 0065-2598.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971209

L26 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:282997 BIOSIS
DOCUMENT NUMBER: PREV199799582200
TITLE: Preclinical studies on combination conjugate vaccines against multiple serotypes of group B streptococci.
AUTHOR(S): **Laude-Sharp, M.**; Fusco, P. C.; D'Ambra, A. J.; Long-Rowe, K.; **Blake, M. S.**; Tai, J. Y.; Michon, F.
CORPORATE SOURCE: North American Vaccine Inc., Beltsville, MD USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1997) Vol. 97, No. 0, pp. 251.
Meeting Info.: 97th General Meeting of the American Society for Microbiology Miami Beach, Florida, USA May 4-8, 1997
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L26 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 1996:25269 HCAPLUS
DOCUMENT NUMBER: 124:66569
TITLE: Group A streptococcal polysaccharide immunogenic compositions and methods
INVENTOR(S): **Blake, Milan S.**; Zabriskie, John B.; Tai, Joseph Y.; **Michon, Francis**
PATENT ASSIGNEE(S): Rockefeller University, USA; North American Vaccine, Inc.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528960	A1	19951102	WO 1995-US4973	19950420

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES,

FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU
LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
SI, SK, TJ, TT, UA
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG

US 5866135	A	19990202	US 1994-231229	19940421
CA 2188284	AA	19951102	CA 1995-2188284	19950420
AU 9522967	A1	19951116	AU 1995-22967	19950420
AU 709797	B2	19990909		
EP 754055	A1	19970122	EP 1995-916479	19950420
EP 754055	B1	20000927		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

CN 1149835	A	19970514	CN 1995-193413	19950420
BR 9507400	A	19971007	BR 1995-7400	19950420
JP 09512276	T2	19971209	JP 1995-527802	19950420
AT 196605	E	20001015	AT 1995-916479	19950420
ES 2151597	T3	20010101	ES 1995-916479	19950420
PL 181037	B1	20010531	PL 1995-316906	19950420
NO 9604413	A	19961217	NO 1996-4413	19961017
FI 9604189	A	19961218	FI 1996-4189	19961018

PRIORITY APPLN. INFO.: US 1994-231229 A 19940421
WO 1995-US4973 W 19950420

AB This invention provides a novel immunogenic compn. and vaccine, processes for producing them and methods for immunization against infectious and disease caused by group A Streptococci. The compns. include **group A streptococcal** polysaccharide covalently **linked** to protein or liposomes to form immunogenic **conjugates**. The method of immunization for this invention comprises administering to an individual an immunogenic amt. of group A polysaccharide. The group A polysaccharide may be administered as a vaccine either on its own, conjugated to proteins or conjugated to liposomes. Addnl., the group A polysaccharides may be assocd. with an adjuvant. This invention is particularly useful for providing both active and passive immunogenic protection for those populations most at risk of contracting group A Streptococcal infections and disease namely adults, pregnant women and in particular infants and children.

DUPLICATE 7

L26 ANSWER 12 OF 16 MEDLINE
ACCESSION NUMBER: 95181865 MEDLINE
DOCUMENT NUMBER: 95181865 PubMed ID: 7876606
TITLE: Group A streptococcus-liposome ELISA antibody titers to group A polysaccharide and opsonophagocytic capabilities of the antibodies.
AUTHOR: Salvadori L G; **Blake M S**; McCarty M; Tai J Y; Zabriskie J B
CORPORATE SOURCE: Laboratory of Clinical Microbiology/Immunology, Rockefeller University, New York, New York 10021.
CONTRACT NUMBER: AI18149 (NIAID)
RR-0102 (NCRR)
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1995 Mar) 171 (3) 593-600.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950419
Last Updated on STN: 19950419
Entered Medline: 19950406

AB Antibodies reactive with **group A** **streptococci** (**GAS**) carbohydrate were studied by ELISA and in an indirect bactericidal assay. The ELISA used **GAS** carbohydrate covalently **bound** to phosphatidylethanolamine incorporated into liposomes so that both precipitating and nonprecipitating antibodies were measured. Sera from children from different geographic areas exhibited marked differences in levels of anti-**GAS** carbohydrate antibody, which increased with age. The antibodies were predominantly of IgG. In bactericidal assays, most of these sera promoted phagocytosis of several type-specific M-positive strains. Opsonization was also related to serum levels of anti-**GAS** carbohydrate antibodies. These opsonizing antibodies were depleted from the serum by absorption of the sera on an N-acetyl-D-glucosamine affinity column. Antibody eluted from this column could partially restore opsonization of **GAS**. Anti-**GAS** carbohydrate antibodies play a major role in these opsonophagocytosis assays.

DUPLICATE 8

L26 ANSWER 13 OF 16 MEDLINE
ACCESSION NUMBER: 94377286 MEDLINE
DOCUMENT NUMBER: 94377286 PubMed ID: 8090587
TITLE: Isolation of lipoprotein-proteoglycan complexes from balloon catheter deendothelialized aortas and the uptake of these complexes by blood monocyte-derived macrophages.
AUTHOR: Ismail N A; Alavi M Z; **Moore S**
CORPORATE SOURCE: Department of Pathology, McGill University, Montreal, Canada.
SOURCE: PATHOLOGY, (1994 Apr) 26 (2) 145-53.
Journal code: 0175411. ISSN: 0031-3025.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941031
Last Updated on STN: 19941031
Entered Medline: 19941020

AB Lipoprotein-Proteoglycan (LP-PG) complexes from the neointima, developed in response to injury, were studied to examine their ability to stimulate lipid accumulation in blood monocyte-derived macrophages (BMDM). LP-PG complexes were extracted from intimal-medial tissues from normal and balloon catheter deendothelialized aortas of normocholesterolemic rabbits, in 0.16 M NaCl for 24 h at 4 degrees C. The extract was purified through an anti-apo-B affinity column. Adsorbed material dissociated with 4 M Gu-HCI buffer was analyzed for lipoproteins (LP) and glycosaminoglycans (GAG). Results demonstrated that LP-PG complexes consisted of apo-B associated with chondroitin sulfate and **hyaluronic** acid. BMDM were incubated with 125I-LP, 125I-LP-NPG (from normal aortas) or 125I-LP-IPG (from injured aortas) for 20 h at 37 degrees C. LP **binding**, internalization and degradation was markedly increased for LP-NPG

and LP-IPG over native LP. Phagocytosis appeared to be the primary route of uptake of LP-PG complexes. Competition experiments indicated that about 40% of the uptake of LP-PG complexes is mediated by the apo-B/E receptor pathway. The scavenger receptor played a minor part in the uptake of LP-PG complexes. Data from this study indicate that LP-PG complexes are present in normal and injured aortas of normocholesterolemic rabbits and these complexes accelerate LP uptake by BMDM more than native LP. Therefore, LP-PG complexes may contribute to lipid accumulation by BMDM, thus generating foam cells. Furthermore, LP-PG complexes prepared from PG of injured aortas are more effective in lipid accumulation than LP-PG complexes from PG of normal aortas.

L26 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:152120 HCAPLUS
DOCUMENT NUMBER: 110:152120
TITLE: The in vitro interactions between serum lipoproteins and proteoglycans of the neointima of rabbit aorta after a single balloon catheter injury
AUTHOR(S): Alavi, Misbahuddin Z.; Richardson, Mary; **Moore, Sean**
CORPORATE SOURCE: Dep. Pathol., McGill Univ., Montreal, PQ, H3A 2B4, Can.
SOURCE: Am. J. Pathol. (1989), 134(2), 287-94
CODEN: AJPAA4; ISSN: 0002-9440
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors studied if the lipoprotein-complexing proteoglycan (LCP) in the neointima covered by regenerated endothelium (NCRE) after balloon catheter-induced endothelial injury differed from that of normal tissue in its ability to bind lipoprotein. LCP isolated from NCRE had a stronger affinity for low-d. lipoprotein and very low-d. lipoprotein than LCP isolated from normal tissue. The relations of the data to atherosclerosis are discussed.

L26 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
ACCESSION NUMBER: 1988:588404 HCAPLUS
DOCUMENT NUMBER: 109:188404
TITLE: Immunogenicity of liposome-**bound hyaluronate** in mice. At least two different antigenic sites on **hyaluronate** are identified by mouse monoclonal antibodies
AUTHOR(S): Fillit, Howard M.; **Blake, Milan;** MacDonald, Christa; McCarty, Maclyn
CORPORATE SOURCE: Lab. Bacteriol. Immunol., Rockefeller Univ., New York, NY, USA
SOURCE: J. Exp. Med. (1988), 168(3), 971-82
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hyaluronate (HA) was previously demonstrated to be immunogenic in rabbits. The immunogenicity of HA in mice was studied. Hyaluronidase-digested streptococcal HA (IA1) covalently linked to liposomes (IA1-liposomes) were produced for immunization. Mice immunized with IA1-liposomes developed measurable serum antibodies to IA1, while mice immunized with IA1 in Freund's adjuvant did not. The mAbs produced by 2 stable hybridomas (10G6 and 5F11) from mice

immunized with IA1-liposomes produced IgG antibody reactive with HA in ELISA. The results confirm that HA is immunogenic and suggest that the mode of presentation of HA is important for the induction of the immune response, and in HA antigenicity. At least 2 different antigenic sites on HA were demonstrated. The 10G6 recognizes a terminal HA antigenic site expressed on IA1-liposomes that contains glucuronic acid in its immunodominant site; 5F11 recognizes an HA antigenic site in which electrostatic forces appear to play a role, is sensitive to ascorbic acid treatment, and is cross-reactive with heparan sulfate.

L26 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 10

ACCESSION NUMBER: 1986:570225 HCAPLUS
DOCUMENT NUMBER: 105:170225
TITLE: Induction of antibodies to hyaluronic acid by immunization of rabbits with encapsulated streptococci
AUTHOR(S): Fillit, Howard M.; McCarty, Maclyn; **Blake, Milan**
CORPORATE SOURCE: Lab. Bacteriol. Immunol., Rockefeller Univ., NY, 10021, USA
SOURCE: J. Exp. Med. (1986), 164(3), 762-76
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The immunogenicity of hyaluronic acid was investigated. Rabbits were immunized with encapsulated group A and C streptococci. Intact long-chain **hyaluronate** was **conjugated** to bovine serum albumin (BSA) for use as antigen in an ELISA. Antibodies to the **hyaluronate**-BSA **conjugate** were detected in peak immune sera. The specificity of the antibodies for both mammalian and streptococcal hyaluronate was shown by inhibition studies. To further confirm the presence of antihyaluronate antibodies, hyaluronidase-digested streptococcal **hyaluronate** was **conjugated** to biotin and used as an antigen in the ELISA. A clear immunization effect was shown for each rabbit by the study of preimmune and postimmunization bleedings. Titers for each rabbit increased by >32-256-fold. Inhibition studies using hyaluronidase-digested hyaluronate and periodate-treated hyaluronate showed that the immunodominant site of antibody reactivity was a terminal glucuronic acid residue. Further studies showed that the carboxyl group of the terminal glucuronide was the major immunoreactive site. Both mammalian and streptococcal hyaluronate inhibited the immune site. Both mammalian and streptococcal hyaluronate inhibited the immune rabbit sera reaction to streptococcal hyaluronate, demonstrating cross-reactivity of these mols. Thus, hyaluronate was shown to be immunogenic in rabbits.

FILE 'HOME' ENTERED AT 15:50:07 ON 27 JUN 2002

Devi, S.
09/853367

27jun02 14:37:47 User219783 Session D1837.1

SYSTEM:OS - ~~DIALOG OneSearch~~

File 35:Dissertation Abs Online 1861-2002/May
(c) 2002 ProQuest Info&Learning
File 65:Inside Conferences 1993-2002/Jun W4
(c) 2002 BLDSC all rts. reserv.
File 77:Conference Papers Index 1973-2002/May
(c) 2002 Cambridge Sci Abs
File 144:Pascal 1973-2002/Jun W4
(c) 2002 INIST/CNRS
File 266:FEDRIP 2002/Apr
Comp & dist by NTIS, Intl Copyright All Rights Res
File 440:Current Contents Search(R) 1990-2002/Jun 27
(c) 2002 Inst for Sci Info
File 348:EUROPEAN PATENTS 1978-2002/Jun W03
(c) 2002 European Patent Office
File 357:Derwent Biotech Res. 1982-2002/Mar W4
(c) 2002 Thomson Derwent & ISI
*File 357: Price changes as of 1/1/02. Please see HELP RATES 357.
Derwent announces file enhancements. Please see HELP NEWS 357.
File 113:European R&D Database 1997
(c)1997 Reed-Elsevier(UK)Ltd All rts reserv
*File 113: This file is closed (no updates)

Set Items Description
--- ----- -----------

Set Items Description
S1 19554 HA(20N)HYALURON??? OR HYALURONATE OR HYALURONIC OR (GROUP(-W)(A OR C))(5N)STREPTOCOCC? OR (GAS OR GCS)(20N)STREPTOCOCC?
S2 2560 S1(20N)(CONJUGAT? OR LINK? OR BOUND OR BIND? OR COUPL?)
S3 37 S2 AND ((PROTEIN? ? OR POLYPROTEIN? ? OR PEPTIDE? ? OR POLYPEPTIDE? ?)(5N)CARRIER? ?)
S4 32 RD (unique items)

_key terms

>>>No matching display code(s) found in file(s): 65, 113

4/3,AB/1 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
(c) 2002 INIST/CNRS. All rts. reserv.

13878396 PASCAL No.: 99-0057128
Prevalence of internalisation-associated gene, prtF1, among persisting group-A streptococcus strains isolated from asymptomatic carriers
NEEMAN R; KELLER N; BARZILAI A; KORENMAN Z; SELA S
Department of Human Microbiology, Sackler School of Medicine, Tel-Aviv University, Israel; Department of Clinical Microbiology, Chaim Sheba Medical Center, Tel-Hashomer Hospital, Israel; Department of Pediatrics, Chaim Sheba Medical Center, Tel-Hashomer Hospital, Israel; Israeli Streptococcal Reference Center, Central Laboratories, Jerusalem, Israel
Journal: Lancet : (British edition), 1998, 352 (9145) 1974-1977
Language: English
Background The failure of antibiotic treatment to eradicate group-A streptococci in up to 30% of patients with pharyngotonsillitis is unexplained. Some strains of group-A streptococci can enter respiratory epithelial cells, where they would be inaccessible to antibiotics unable to penetrate the cell membrane, such as penicillins. The fibronectin-*binding"** proteins, F1 and Sfbl, are needed for this process. We

hypothesised, therefore, that an intracellular reservoir of *group"**-*A"** *streptococci"** could account, at least partly, for failure to eradicate throat carriage, and that the presence of the gene for fibronectin-*binding"** protein (F1) might be linked to the ability of a strain to persist in the throat after therapy. Methods We investigated the frequency of prtF1-containing strains among 67 patients with pharyngotonsillitis. All patients were clinically cured, although 13 of them continued to carry group-A streptococci in the throat during or after therapy. To distinguish between persisting and recolonising strains, isolates from the 13 patients were serologically tested and compared by polymorphic DNA-amplification technique. Findings 12 (92%) of the 13 patients with symptomless carriage had prtF1-containing strains in the throat, compared with 16 (30%) of the 54 patients with successful eradication (p=0.0001). Three of the 13 eradication-failure patients were recolonised with strains that differed from the pretreatment strains. Nine of the ten (90%) persisting strains carried prtF1 (p=0.0009). Interpretation Our findings suggest that protein-F1-mediated entry to cells is involved in the causative process of the carriage state.

4/3,AB/2 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

12925063 PASCAL No.: 97-0194353
Description of an albumin binding activity for Streptococcus suis serotype 2
QUESSY S; BUSQUE P; HIGGINS R; JACQUES M; DUBREUIL J D
Laboratoire d hygiene veterinaire et alimentaire, Agriculture et Agro-alimentaire Canada, 3400 Casavant ouest, St-Hyacinthe, Quebec J2S 8E3, Canada; Groupe de Recherche sur les Maladies Infectieuses du Porc, Faculte de medecine veterinaire, Universite de Montreal, C.P. 5000, St-Hyacinthe, Quebec J2S 7C6, Canada
Journal: FEMS microbiology letters, 1997, 147 (2) 245-250
Language: English Summary Language: English
 This study was undertaken to investigate the binding activity of Streptococcus suis serotype 2 to albumin. Using flow cytometry we observed a binding activity of S. suis to albumin for virulent as well as for avirulent isolates. Western immunoblots analysis revealed that a 39-kDa S. suis protein was responsible, at least in part, for this *binding"** activity. This protein showed high N-terminal homology (95.6% for the first 23 residues) with a *group"** *A"** *Streptococcus"** glyceraldehyde-3-phosphate dehydrogenase. Furthermore, the addition of albumin to the culture broth resulted in an increase in the virulence of S. suis strains in mice. These results suggest that an interaction with albumin could play a role in the pathogenesis of S. suis serotype 2 infections.

4/3,AB/3 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

11699334 PASCAL No.: 94-0561759

M12 protein from Streptococcus pyogenes is a receptor for immunoglobulin G3 and human albumin
RETNONINGRUM D S; CLEARY P P
Univ. Minnesota, dep. microbiology, Minneapolis MN 55455, USA
Journal: Infection and immunity, 1994, 62 (6) 2387-2394
Language: English
We previously showed that M12 protein from opacity factor-negative *Streptococcus"** pyogenes (*group"** *A"** *streptococci"**) CS24 is responsible for immunoglobulin G3 (IgG3) *binding"** activity. Here, we report that this M protein *binds"** human serum albumin (HSA). Deletion analysis showed that the C repeats are sufficient for binding HSA, although upstream regions may be required for optimal binding. Like protein G, IgG3 and HSA bind to independent domains in the M protein. Experiments showed that bound IgG3 did not inhibit HSA binding to the M protein. The interaction between M12 protein and HSA is specific. M12 protein does not bind chicken egg and bovine serum albumins

4/3,AB/4 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal
(c) 2002 INIST/CNRS. All rts. reserv.

10399123 PASCAL No.: 92-0602596
Isolation and molecular characterization of a novel albumin-binding protein from group G streprococci
SJOEBRING U
Univ. Lund, dep. medical microbiology, 22362 Lund, Sweden
Journal: Infection and immunity, 1992, 60 (9) 3601-3608
Language: English
Many streptococcal strains are known to hind the two most abundant plasma proteins, namely, immunoglobulin G and albumin. Protein G isolated from *group"** *C"** and G *streptococci"** has been demonstrated to have separate *binding"** regions for each of these proteins. However, some group G streptococcal strains *bind"** only serum albumin. This report describes the isolation of a 48-kDa albumin-binding protein from such a strain (DG12). The affinity constant of this protein for human serum albumin was determined to be 5x10 SUP 9 M SUP - SUP 1 , and the protein interacted strongly also with serum albumin from several other mammalian species

4/3,AB/5 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2002 Inst for Sci Info. All rts. reserv.

14084171 Document Delivery Available: 000175514700034 References: 21
TITLE: Carriers for enzymatic attachment of glycosaminoglycan chains to peptide
AUTHOR(S): Takagaki K; Ishido K; Kakizaki I; Iwafune M; Endo M (REPRINT)
AUTHOR(S) E-MAIL: endo-m@cc.hirosaki-u.ac.jp
CORPORATE SOURCE: Hirosaki Univ, Dept Biochem, 5 Zaifu Cho/Hirosaki/Aomori 0368562/Japan/ (REPRINT); Hirosaki Univ, Dept Biochem, /Hirosaki/Aomori 0368562/Japan/
PUBLICATION TYPE: JOURNAL
PUBLICATION: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, 2002, V 293, N1 (APR 26), P220-224
GENUINE ARTICLE#: 550QX
PUBLISHER: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN

DIEGO, CA 92101-4495 USA
ISSN: 0006-291X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: In the previous study, we have found that the endo-beta-xylosidase from Patinopecten had the attachment activities of glycosaminoglycan (GAG) chains to *peptide"**. As artificial *carrier"** substrates for this reaction. synthesis of various GAG chains having the *linkage"** region tetrasaccharide. GlcAbeta1-3Galbeta1-3Galbeta1-4Xyl, between GAG chain and core protein of proteoglycan was investigated. *Hyaluronic"** acid (*HA"**), chondroitin (Ch), chondroitin 4-sulfate (Ch4S). chondroitin 6-sulfate (Ch6S), and desulfated dermatan sulfate (desulfated DS) as donors and the 4-metylumbelliferone (MU)-labeled hexasaccharide having the linkage region tetrasaccharide at its reducing terminals (MU-hexasaccharide) as an acceptor were subjected to a transglycosylation reaction of testicular hyaluronidase. The products were analyzed by high-performance liquid chromatography and enzyme digestion, and the results indicated that HA. Ch, Ch4S, Ch6S. and desulfated DS chains elongated by the addition of disaccharide units to the nonreducing terminal of MU-hexasaccharide. It was possible to custom-synthesize various GAG chains having the linkage region tetrasaccharide as carrier substrates for enzymatic attachment of GAG chains to peptide. (C) 2002 Elsevier Science (USA). All rights reserved.

4/3,AB/6 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2002 Inst for Sci Info. All rts. reserv.

12906550 References: 36
TITLE: Decrease of the adhesion of Streptococcus suis serotype 2 mutants to embryonic bovine tracheal cells and porcine tracheal rings
AUTHOR(S): Brassard J; Gottschalk M; Quessy S (REPRINT)
AUTHOR(S) E-MAIL: sylvain.quessy@umontreal.ca
CORPORATE SOURCE: Univ Montreal, Grp Rech Malad Infect Porc, CP 5000/St Hyacinthe/PQ J2S 7C6/Canada/ (REPRINT); Univ Montreal, Grp Rech Malad Infect Porc, /St Hyacinthe/PQ J2S 7C6/Canada/
PUBLICATION TYPE: JOURNAL
PUBLICATION: CANADIAN JOURNAL OF VETERINARY RESEARCH-REVUE CANADIENNE DE RECHERCHE VETERINAIRE, 2001, V65, N3 (JUL), P156-160
GENUINE ARTICLE#: 456HV
PUBLISHER: CANADIAN VET MED ASSOC, 339 BOOTH ST ATTN: KIMBERLY ALLEN-MCGILL, OTTAWA, ONTARIO K1R 7K1, CANADA
ISSN: 0830-9000
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Streptococcus suis is an important swine pathogen that may be present in the tonsils of rigs that show no signs of illness. Because adhesion to host cells may be important in the carrier state, this study was undertaken to investigate adhesion to host cells by S. suis mutant strains defective in expression of a 39-kDa protein. Mutant strains of S, suis were generated by transposon Tn916 mutagenesis and were tested for adhesion to embryonic bovine tracheal cells and porcine tracheal rings. Compared with the parent strain, there was a significant reduction in adherence of 3 mutant strains to both bovine tracheal cells and porcine tracheal rings.

4/3,AB/7 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12360712 References: 72
TITLE: Topological organization of the hyaluronan synthase from Streptococcus pyogenes
AUTHOR(S): Heldermon C; DeAngelis PL; Weigel PH (REPRINT)
AUTHOR(S) E-MAIL: paul-weigel@OUHSC.edu
CORPORATE SOURCE: Univ Oklahoma, Dept Biochem & Mol Biol, /Oklahoma City//OK/73190 (REPRINT); Univ Oklahoma, Dept Biochem & Mol Biol, /Oklahoma City//OK/73190
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF BIOLOGICAL CHEMISTRY, 2001, V276, N3 (JAN 19), P 2037-2046
GENUINE ARTICLE#: 394MN
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA
ISSN: 0021-9258
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Since we first reported (DeAngelis, P, L,, Papaconstantinou, J,, and Weigel, P, H. (1993) J, Biol. Chem. 268, 19181-19184) the cloning of the *hyaluronan"** (*HA"**) synthase from Streptococcus pyogenes (spHAS), numerous membrane-*bound"** *HA"** synthases have been discovered in both prokaryotes and eukaryotes. The HASs are unique among enzymes studied to date because they mediate 6-7 discrete functions in order to assemble a polysaccharide containing hetero-disaccharide units and simultaneously effect translocation of the growing HA chain through the plasma membrane. To understand how the relatively small spHAS performs these various functions, we investigated the topological organization of the protein utilizing fusion analysis with two reporter enzymes, alkaline phosphatase and beta -galactosidase, as well as several other approaches. From these studies, we conclude that the NH2 terminus and the COOH terminus, as well as the major portion of a large central domain are localized intracellularly, The first two predicted membrane domains were confirmed to be transmembrane domains and give rise to a very small extracellular loop that is inaccessible to proteases, Several regions of the large internal central domain appear to be associated with, but do not traverse, the membrane. Following the central domain, there are two additional transmembrane domains connected by a second small extracellular loop that also is inaccessible to proteases, The COOH-terminal similar to 25% of spHAS also contains a membrane domain that does not traverse the membrane and may contain extensive re-entrant loops or amphipathic helices, Numerous membrane associations of this latter COOH-terminal region and the central domain may be required to create a pore-like structure through which a growing HA chain can be extruded to the cell exterior. Based on the high degree of similarity among Class I HAS family members, these enzymes may have a similar topological organization for their spHAS-related domains.

4/3,AB/8 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01291711
Immunostimulating carrier for vaccines
Immunostimulierender Trager fur Impfstoffe

Support immunostimulant pour des vaccins
PATENT ASSIGNEE:
Petrovax, Inc., (2320190), 147 North Main Street, P.O. Box 201, South Deerfield, MA 01373, (US), (Applicant designated States: all)
INVENTOR:
Petrov, Rem V., Building, Flat 86, Academician Zelinski Street, House 38, Moscow 117334, (RU)
Khaitov, Rakhim M., House 39, Flat 120, Bolshaja Grusinskaja Street, Moscow 123056, (RU)
Ataullakhanov, Ravshan I., Building 1, Flat 262, Severodvinskaja Street, House 13, Moscow 129224, (RU)
Nekrasov, Arkady V., House 4, Building 1, Flat 420, Kuncevskaja Street, Moscow 121353, (RU)
Daugalievea, Emma K., House 29, Building 1, Flat 354, Krilatskaja Street, Moscow 121614, (RU)
LEGAL REPRESENTATIVE:
Perry, Robert Edward et al (41331), GILL JENNINGS & EVERY Broadgate House 7 Eldon Street, London EC2M 7LH, (GB)
PATENT (CC, No, Kind, Date): EP 1108738 A2 010620 (Basic)
EP 1108738 A3 010725
APPLICATION (CC, No, Date): EP 2000125257 940912;
PRIORITY (CC, No, Date): US 120001 930910; US 207486 940307
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; SI
RELATED PARENT NUMBER(S) - PN (AN):
EP 789586 (EP 94929200)
INTERNATIONAL PATENT CLASS: C08G-073/06; C12N-011/08; A61K-039/00; A61K-039/385; A61K-045/00

ABSTRACT EP 1108738 A3
A polymer that has utility as immunostimulating carrier is a copolymer of ethylenepiperazine N-oxide and N-(carboxymethyl)ethylene-piperazinium.
ABSTRACT WORD COUNT: 17
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200125	187
SPEC A	(English)	200125	4862
Total word count - document A			5049
Total word count - document B			0
Total word count - documents A + B			5049

4/3,AB/9 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01193213
NUCLEIC ACID TRANSPORTERS AND MEDICINAL COMPOSITIONS FOR GENE THERAPY
NUKLEINSAURE-TRANSPORTER UND MEDIZINISCHE ZUSAMMENSETZUNGEN FUR DIE GENTHERAPIE
TRANSPORTEURS D'ACIDE NUCLEIQUE ET COMPOSITIONS MEDICINALES POUR LA THERAPIE GENIQUE
PATENT ASSIGNEE:

HISAMITSU PHARMACEUTICAL CO. INC., (444625), 408, Tashirodaikan-machi, Tosu-shi Saga 841-0017, (JP), (Applicant designated States: all)
INVENTOR:
GOTO, Takeshi, Tsukuba Lab.of Hisamit Phar. Co Inc, 25-11, Kannondai 1-chome, Tsukuba-shi, Ibaraki 305-0856, (JP)
YONEMURA, K., Tsukuba Lab.of Hisamit Phar. Co. Inc, 25-11, Kannondai 1-chome, Tsukuba-shi, Ibaraki 305-0856, (JP)
KUWAHARA, T., Tsukuba Lab. of Hisamit Phar. Co.Inc, 25-11, Kannondai 1-chome, Tsukuba-shi Ibaraki 305-0856, (JP)
OYA, M., Tsukuba Lab. of Hisamitsu Pharm. Co. Inc., 25-11, Kannondai 1-chome, Tsukuba-shi, Ibaraki 30 5-0856, (JP)
AKIYAMA, K., Tsukuba Lab. of Hisamit Phar. Co. Inc, 25-11, Kannondai 1-chome, Tsukuba-shi, Ibaraki 305-0856, (JP)
LEGAL REPRESENTATIVE:
Grunecker, Kinkeldey, Stockmair & Schwanhausser Anwaltssozietat (100721), Maximilianstrasse 58, 80538 Munchen, (DE)

PATENT (CC, No, Kind, Date): EP 1132099 A1 010912 (Basic)
WO 200029031 000525
APPLICATION (CC, No, Date): EP 99972111 991117; WO 99JP6415 991117
PRIORITY (CC, No, Date): JP 98328126 981118
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-048/00

ABSTRACT EP 1132099 A1
A novel nucleic acid carrier and a pharmaceutical composition for gene therapy are disclosed. The nucleic acid carrier of this invention is characterized by containing a polypeptide comprising diaminobutyric acid with a suitable number of residues and/or a pharmaceutically acceptable salt thereof. The nucleic acid carrier of this invention can form a complex with a variety of therapeutic genes that is safe and has extremely low immunogenicity (the pharmaceutical composition of this invention); and it can allow the therapeutic gene to be introduced into cells efficiently and safely whereby high expression of the gene in the cells can be realized.
ABSTRACT WORD COUNT: 101
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200137	139
SPEC A	(English)	200137	9118
Total word count - document A			9257
Total word count - document B			0
Total word count - documents A + B			9257

4/3,AB/10 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01076285
Pharmaceutical composition of hedgehog proteins and use thereof
Pharmaceutische Zusammensetzungen von Hedgehog-Proteinen und deren Verwendung
Compositions pharmaceutiques contenant des proteines Hedgehog, et leur

utilisation
PATENT ASSIGNEE:
Roche Diagnostics GmbH (HRB 3962 - vormals Boehringer Mannheim GmbH), (2638981), Sandhofer Strasse 116, 68305 Mannheim, (DE), (Applicant designated States: all)
INVENTOR:
Lang, Kurt, 10 Langoner Strasse, 82377 Penzberg, (DE)
Papadimitriou, Apollon, 38a Bachstrass, 83673 Bichl, (DE)
LEGAL REPRESENTATIVE:
Horner, Martin Grenville et al (45941), Cruikshank & Fairweather 19 Royal Exchange Square, Glasgow G1 3AE Scotland, (GB)
PATENT (CC, No, Kind, Date): EP 947201 A1 991006 (Basic)
APPLICATION (CC, No, Date): EP 99101642 990204;
PRIORITY (CC, No, Date): EP 98101893 980204; EP 98104416 980312
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-047/48; A61K-009/16; A61K-038/17

ABSTRACT EP 947201 A1
A pharmaceutical composition of a hedgehog protein which is characterized in that the hedgehog *protein"** is bound to a hydrophilic *carrier"** that is biocompatible and biodegradable wherein the carrier is a polymer which
- binds the hedgehog *protein"** as a negatively-charged *carrier"** as a result of ionic interactions,
- does not denature the hedgehog *protein"** when it binds to the *carrier"**,
- contains at least 0.1 to 2 negatively-charged residues per monomer under neutral conditions,
- contains the charge in the form of acidic groups,
- has an average molecular weight of at least 50,000 Da
- and contains no agarose reversibly and actively releases hedgehog *proteins"** in vivo from a *carrier"** in a delayed manner.
ABSTRACT WORD COUNT: 117
NOTE:
Figure number on first page: NONE
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9940	534
SPEC A	(English)	9940	3788
Total word count - document A			4322
Total word count - document B			0
Total word count - documents A + B			4322

4/3,AB/11 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00831037
NOVEL PEPTIDES FOR USE IN TREATMENT OF T-CELL MEDIATED CARTILAGE DESTRUCTION IN AUTOIMMUNE DISEASES
NEUE PEPTIDE ZUR VERWENDUNG BEI BEHANDLUNG VON DURCH T-ZELLEN VERMITTELTER KNORPELZERSTORUNGIN AUTOIMMUNKRANKHEITEN
NOUVEAUX PEPTIDES UTILISES DANS LE TRAITEMENT DE LA DESTRUCTION DU CARTILAGE INDUITE PAR LES LYMPHOCYTES T DANS LES MALADIES

AUTO-IMMUNITAIRES
PATENT ASSIGNEE:
Akzo Nobel N.V., (200754), Velperweg 76, 6824 BM Arnhem, (NL),
(Proprietor designated states: all)
INVENTOR:
VERHEIJDEN, Gijsbertus, Franciscus, Maria, Heischouw 7, NL-5345 XT Oss, (NL)
BOOTS, Anna, Maria, Helena, Verlengde Torenstraat 10, NL-5366 AV Megen, (NL)
LEGAL REPRESENTATIVE:
Ogilvie-Emanuelson, Claudia Maria et al (80441), Patent Department Pharma N.V. Organon P.O. Box 20, 5340 BH Oss, (NL)
PATENT (CC, No, Kind, Date): EP 833842 A1 980408 (Basic)
EP 833842 B1 990929
WO 9700270 970103
APPLICATION (CC, No, Date): EP 96920822 960617; WO 96EP2605 960617
PRIORITY (CC, No, Date): EP 95201656 950619
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C07K-014/47; A61K-038/10; A61K-038/16
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9939	369
CLAIMS B	(German)	9939	348
CLAIMS B	(French)	9939	393
SPEC B	(English)	9939	4311
Total word count - document A			0
Total word count - document B			5421
Total word count - documents A + B			5421

4/3,AB/12 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00763661
USE OF CYTADHERENCE PEPTIDES FOR USE IN MODIFYING MUTUAL ADHESION AMONG EUKARYOTIC CELLS
VERWENDUNG VON ZELLADHASIONS-PEPTIDEN ZUR MODIFIKATION DES HAFTUNGSVERMOGENS EUKARYONTISCHER ZELLEN UNTEREINANDER
USAGE DES PEPTIDES D'ADHESION CELLULAIRE DESTINES A MODIFIER LE POUVOIR D'ADHESION INTERCELLULAIRE DE CELLULES EUCARYOTES
PATENT ASSIGNEE:
Beiersdorf Aktiengesellschaft, (417831), Unnastrasse 48, D-20253 Hamburg, (DE), (Proprietor designated states: all)
INVENTOR:
EICHNER, Wolfram, Pferdeweg 35, D-21266 Jesteburg, (DE)
KOCK, Katharina, Theodor-Storm-Strasse 9, D-22869 Schenefeld, (DE)
MIELKE, Heiko, Fischbeker Strasse 22, D-21629 Neu Wulmstorf, (DE)
DOERSCHNER, Albrecht, Schanzenstrasse 107, D-20357 Hamburg, (DE)
LEGAL REPRESENTATIVE:
UEXKULL & STOLBERG (100011), Patentanwalte Beselerstrasse 4, 22607 Hamburg, (DE)
PATENT (CC, No, Kind, Date): EP 777689 A1 970611 (Basic)
EP 777689 B1 000329

WO 9606114 960229
APPLICATION (CC, No, Date): EP 95930443 950808; WO 95EP3135 950808
PRIORITY (CC, No, Date): DE 4430601 940822
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IE; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: C07K-014/78; C07K-017/02; A61K-038/39; C12N-005/08; A61L-027/00
NOTE:
No A-document published by EPO
Figure number on first page: 1
LANGUAGE (Publication,Procedural,Application): German; German; German
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200013	887
CLAIMS B	(German)	200013	764
CLAIMS B	(French)	200013	864
SPEC B	(German)	200013	7998
Total word count - document A			0
Total word count - document B			10513
Total word count - documents A + B			10513

4/3,AB/13 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00707514
Collagen-based injectable drug delivery system and its use
Injizierbares Verabreichungssystem fur Arzneistoffe auf Kollagen-Basis und seine Verwendung
Systeme injectable pour la delivrance d'un medicament a base de collagene et son utilisation

PATENT ASSIGNEE:
Cohesion Technologies, Inc., (2543710), 2500 Faber Place, Palo Alto, CA 94303, (US), (Proprietor designated states: all)
INVENTOR:
Rosenblatt, Joel S., 2651 South Court, Palo Alto, CA 94306, (US)
Berg, Richard A., 660 South Springer Road, Los Altos, CA 94024, (US)
LEGAL REPRESENTATIVE:
Ayers, Martyn Lewis Stanley (42851), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5LX, (GB)

PATENT (CC, No, Kind, Date): EP 671165 A2 950913 (Basic)
EP 671165 A3 951122
EP 671165 B1 010411
APPLICATION (CC, No, Date): EP 95101589 950206;
PRIORITY (CC, No, Date): US 193600 940209
DESIGNATED STATES: CH; DE; FR; GB; IT; LI
INTERNATIONAL PATENT CLASS: A61K-009/00; A61K-047/42; A61M-037/00

ABSTRACT EP 671165 A2
Drugs are delivered in a sustained manner from an in vivo depot which is formed from a collagen-based injectable composition. The injectable composition is fluid when injected but undergoes crosslinking in situ to form a crosslinked collagen matrix which encloses the drug to be released. The composition also includes a flexible chain polymer which is similarly charged to the precrosslinked collagen. This flexible chain polymer is enclosed in the matrix as well when the matrix forms and alters the effective porosity of the matrix. The drug diffuses out of the matrix at a rate which depends upon the matrix's effective porosity. (see

image in original document)
ABSTRACT WORD COUNT: 108
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB95	512
CLAIMS B	(English)	200115	937
CLAIMS B	(German)	200115	928
CLAIMS B	(French)	200115	1105
SPEC A	(English)	EPAB95	7338
SPEC B	(English)	200115	6966
Total word count - document A			7851
Total word count - document B			9936
Total word count - documents A + B			17787

4/3,AB/14 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00692899
COMPOUNDS FOR THE PREVENTION AND TREATMENT OF HELMINTH INFECTIONS
VERBINDUNGEN ZUR VERHUTUNG UND BEHANDLUNG VON HELMINTHINFEKTIONEN
COMPOSES PERMETTANT DE PREVENIR ET DE TRAITER DES INFECTIONS PROVOQUEES PAR UN HELMINTHE
PATENT ASSIGNEE:
Petrovax, Inc., (2320190), 147 North Main Street, P.O. Box 201, South Deerfield, MA 01373, (US), (Proprietor designated states: all)
INVENTOR:
PETROV, Rem V., House 38, Building 8, Flat 86, Academician Zelinski Street, Moscow, 117334, (RU)
KHAITOV, Rakhim M., House 39,Flat 120, Bolshaja Grusinskaja Street, Moscow, 123056, (RU)
ATAULLAKHANOV, Ravshan I., House 13, Building 1, Flat 262, Severodvinskaja Street, Moscow, 129224, (RU)
NEKRASOV, Arkady V., House 4, Building 1,Flat 420, Kuncevskaja Street, Moscow, 121353, (RU)
DAUGALIEVA, Emma K., House 29, Building 1, Flat 354, Krilatskaja Street, Moscow, 121614, (RU)
LEGAL REPRESENTATIVE:
Perry, Robert Edward et al (41331), GILL JENNINGS & EVERY Broadgate House 7 Eldon Street, London EC2M 7LH, (GB)
PATENT (CC, No, Kind, Date): EP 789586 A1 970820 (Basic)
EP 789586 A1 990526
EP 789586 B1 010704
WO 9507100 950316
APPLICATION (CC, No, Date): EP 94929200 940912; WO 94US10346 940912
PRIORITY (CC, No, Date): US 120001 930910; US 207486 940307
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 1108738 (EP 2000125257)
INTERNATIONAL PATENT CLASS: A61K-039/00; A61K-039/385; A61K-045/00; C07D-403/00; C07D-241/02; C07D-233/00; C12N-011/08
NOTE:

No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200127	178
CLAIMS B	(German)	200127	165
CLAIMS B	(French)	200127	196
SPEC B	(English)	200127	7804
Total word count - document A			0
Total word count - document B			8343
Total word count - documents A + B			8343

4/3,AB/15 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00686989
Glycosaminoglycan-synthetic polymer conjugates.
Glukosominoglukan-synthetische-Polymer-Konjugaten.
Conjugues de glycosominoglucanes et de polymeres synthetiques.
PATENT ASSIGNEE:
COLLAGEN CORPORATION, (255151), 2500 Faber Place, Palo Alto, California 94303, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;IT;LI;NL;SE)
INVENTOR:
Rhee, Woonza M., 3845 La Donna Ave., Palo Alto, CA 94306, (US)
Berg, Richard A., 660 South Springer Road, Los Altos, CA 94024, (US)
LEGAL REPRESENTATIVE:
Schwan, Gerhard, Dipl.-Ing. (10931), Elfenstrasse 32, D-81739 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 656215 A1 950607 (Basic)
APPLICATION (CC, No, Date): EP 94117227 941101;
PRIORITY (CC, No, Date): US 146843 931103
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-047/48; A61L-027/00; A61L-031/00;

ABSTRACT EP 656215 A1
Pharmaceutically acceptable, nonimmunogenic compositions are formed by covalently binding glycosaminoglycans or derivatives thereof, to hydrophilic synthetic polymers via specific types of chemical bonds to provide biocompatible *conjugates"**. Useful glycosaminoglycans include *hyaluronic"** acid, the chondroitin sulfates, keratan sulfate, chitin and heparin, each of which is chemically derivatized to react with a hydrophilic synthetic polymer. The conjugate comprising a glycosaminoglycan covalently bound to a hydrophilic synthetic polymer may be further bound to collagen to form a three component conjugate having different properties. The hydrophilic synthetic polymer may be polyethylene glycol and derivatives thereof having an average molecular weight over a range of from about 100 to about 100,000. The compositions may include other components such as fluid, pharmaceutically acceptable carriers to form injectable formulations, and/or biologically active proteins such as growth factors or cytokines.
ABSTRACT WORD COUNT: 134

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count

CLAIMS A	(English)	EPAB95	1084
SPEC A	(English)	EPAB95	9832
Total word count - document A			10916
Total word count - document B			0
Total word count - documents A + B			10916

4/3,AB/16 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00643918
TGF-BETA FORMULATION FOR INDUCING BONE GROWTH
TGF-BETA ZUSAMMENSETZUNG ZUM HERBEIFUHREN VON KNOCHENWACHSTUM
FORMULATION DU FACTEUR DE CROISSANCE DE TRANSFORMATION BETA PROVOQUANT LA CROISSANCE DES OS
PATENT ASSIGNEE:
GENENTECH, INC., (210485), 460 Point San Bruno Boulevard, South San Francisco, CA 94080-4990, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
AMMANN, Arthur, J., 104 Dominican Drive, San Rafael, CA 94901, (US)
BECK, Steven L., 1871 Orange Tree Lane, Mountain View CA 94040, (US)
NGUYEN, Tue, H., 1816 Canyon Oak Court, San Mateo, CA 94402, (US)
ONGPIPATTANAKUL, Boonsri, Apartment 202, 10 De Sable Road, San Mateo, CA 94402, (US)
RUDMAN, Christopher, G., 425 Beacon, San Francisco, CA 94131, (US)
LEGAL REPRESENTATIVE:
Walton, Sean Malcolm et al (77071), Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 679097 A1 951102 (Basic)
EP 679097 B1 970528
WO 9415653 940721
APPLICATION (CC, No, Date): EP 94906606 940111; WO 94US409 940111
PRIORITY (CC, No, Date): US 3365 930112
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-038/30;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB97	385
CLAIMS B	(German)	EPAB97	359
CLAIMS B	(French)	EPAB97	443
SPEC B	(English)	EPAB97	16157
Total word count - document A			0
Total word count - document B			17344
Total word count - documents A + B			17344

4/3,AB/17 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00620554
ANTIGEN OF HYBRID M *PROTEIN"** AND *CARRIER"** FOR GROUP A STREPTOCOCCAL

VACCINE
ANTIGENE DES HYBRIDEN M-PROTEINS UND TRAGER FUR GRUPPE A STREPTOKOKKENIMPFSTOFF
ANTIGENE DE LA PROTEINE M HYBRIDE ET PORTEUR DESTINE AU VACCIN ANTI-STREPTOCOCCIQUE DU GROUPE A
PATENT ASSIGNEE:
THE UNIVERSITY OF TENNESSEE RESEARCH CORPORATION, (345011), Suite 415, Communications Building, Knoxville, Tennessee 37966-0344, (US), (Proprietor designated states: all)
INVENTOR:
DALE, James, B., 72 Lombardy Road, Memphis, TN 38111, (US)
LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance et al (61531), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 618813 A1 941012 (Basic)
EP 618813 A1 970521
EP 618813 B1 020109
WO 9406465 940331
APPLICATION (CC, No, Date): EP 93922202 930915; WO 93US8704 930915
PRIORITY (CC, No, Date): US 945860 920916
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/02; A61K-039/09; C07K-002/00; C07H-015/12; C07K-014/315; C07K-014/245
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200202	318
CLAIMS B	(German)	200202	290
CLAIMS B	(French)	200202	340
SPEC B	(English)	200202	9441
Total word count - document A			0
Total word count - document B			10389
Total word count - documents A + B			10389

4/3,AB/18 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00556655
CYTOKINE-INDUCED PROTEIN, TSG-6, DNA CODING THEREFOR AND USES THEREOF
CYTOKIN-INDUZIERTES PROTEIN, TSG-6, SEINE DNA UND VERWENDUNG
POTEINE INDUITE PAR LA CYTOKINE, ADN TSG-6 CODANT POUR CETTE PROTEINE ET SES UTILISATIONS
PATENT ASSIGNEE:
NEW YORK UNIVERSITY, (300275), 550 First Avenue, Room MSB 153, New York, NY 10016, (US), (Proprietor designated states: all)
INVENTOR:
LEE, Tae, Ho, 206 Pleasant View Drive, Piscatawa, NJ 08855, (US)
WISNIEWSKI, Hans-Georg, 55 Omni Parc Drive, Spring Valley, NY 10977, (US)
VILCEK, Jan, 180 E. 79th Street, New York, NY 10021, (US)
LEGAL REPRESENTATIVE:
Rinuy, Santarelli (100891), 14, avenue de la Grande Armee, 75017 Paris, (FR)
PATENT (CC, No, Kind, Date): EP 567575 A1 931103 (Basic)

EP 567575 A1 950426
EP 567575 B1 991013
WO 9212175 920723
APPLICATION (CC, No, Date): EP 92904669 920114; WO 92US333 920114
PRIORITY (CC, No, Date): US 642312 910114
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-014/47; C12P-021/02; C12Q-001/68; G01N-033/53
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9941	822
CLAIMS B	(German)	9941	811
CLAIMS B	(French)	9941	943
SPEC B	(English)	9941	24723
Total word count - document A			0
Total word count - document B			27299
Total word count - documents A + B			27299

4/3,AB/19 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00522765
Composition for revitalizing scar tissue
Zusammensetzung zur Revitalisierung von Nerbgewebe
Composition pour revitaliser le tissu cicatrise
PATENT ASSIGNEE:
C.R. BARD, INC., (247301), 730 Central Avenue, Murray Hill New Jersey 07974, (US), (applicant designated states: DE;ES;FR;GB;IT)
INVENTOR:
Lee, Clarence C., 1141 Kelvington Way, Lilburn, Georgia 30247, (US)
LEGAL REPRESENTATIVE:
Sternagel, Hans-Gunther, Dr. et al (46853), Patentanwalte Dr. Michael Hann, Dr. H.-G. Sternagel, Dr. H. Dorries, Sander Aue 30, 51465 Bergisch Gladbach, (DE)
PATENT (CC, No, Kind, Date): EP 526756 A1 930210 (Basic)
EP 526756 B1 970502
APPLICATION (CC, No, Date): EP 92111651 920709;
PRIORITY (CC, No, Date): US 728171 910710
DESIGNATED STATES: DE; ES; FR; GB; IT
INTERNATIONAL PATENT CLASS: A61K-038/18; A61K-038/39;

ABSTRACT EP 526756 A1
A composition is provided that is effective in revitalizing scar tissue by introducing a bioactive substance having angiogenic activity into the scar tissue. The bioactive substance can be introduced by itself, or it can be introduced into the scar tissue in a timed release form. The present invention is effective in treating stress urinary incontinence or localized muscular dysfunction.
ABSTRACT WORD COUNT: 61

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count

CLAIMS A	(English)	EPABF1	322
CLAIMS B	(English)	EPAB97	323
CLAIMS B	(German)	EPAB97	286
CLAIMS B	(French)	EPAB97	399
SPEC A	(English)	EPABF1	3867
SPEC B	(English)	EPAB97	3859
Total word count - document A			4189
Total word count - document B			4867
Total word count - documents A + B			9056

4/3,AB/20 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00508048
IMPROVED VACCINE COMPOSITIONS
VERBESSERTE VAKZINZUSAMMENSETZUNG
VACCIN AMELIORE
PATENT ASSIGNEE:
NORTH AMERICAN VACCINE, INC., (1439710), 10900 Hamon Street, Montreal, Quebec H3M 3A2, (CA), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
PENNEY, Christopher, L., 20 Allenbrooke, Dollard des Ormeaux, Quebec H9A 2S5, (CA)
MICHON, Francis, 429 Nelson Street, Ottawa, Ontario K1N 7S6, (CA)
JENNINGS, Harold, J., 2049 Woodglen Crescent, Gloucester, Ontario K1J 6G6, (CA)
LEGAL REPRESENTATIVE:
Laufhutte, Dieter, Dr.-Ing. et al (61841), Lorenz-Seidler-Gossel Widenmayerstrasse 23, D-80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 549617 A1 930707 (Basic)
EP 549617 B1 960327
WO 9204915 920402
APPLICATION (CC, No, Date): EP 91915418 910912; WO 91CA326 910912
PRIORITY (CC, No, Date): US 583372 900917
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/39; A61K-039/095; A61K-047/48;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB96	667
CLAIMS B	(German)	EPAB96	576
CLAIMS B	(French)	EPAB96	736
SPEC B	(English)	EPAB96	6136
Total word count - document A			0
Total word count - document B			8115
Total word count - documents A + B			8115

4/3,AB/21 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00473242

Connective tissue prosthesis.
Bindegewebeprothesen.
Prothese pour tissu conjonctif.
PATENT ASSIGNEE:
UNITED STATES SURGICAL CORPORATION, (304772), 150 Glover Avenue, Norwalk, Connecticut 06856, (US), (applicant designated states: DE;FR;GB)
INVENTOR:
Kaplan, Donald S., 7 White Oak Lane, Weston, CT 06883, (US)
Kennedy, John, 61 Rowland Street, Stratford, CT 06497, (US)
Muth, Ross R., 97 Clearview Drive, Brookfield, CT 06804, (US)
LEGAL REPRESENTATIVE:
Marsh, Roy David et al (45988), Hoffmann Eitle & Partner Patent- und Rechtsanwalte Arabellastrasse 4 Postfach 81 04 20, W-8000 Munchen 81, (DE)
PATENT (CC, No, Kind, Date): EP 485986 A1 920520 (Basic)
APPLICATION (CC, No, Date): EP 91119352 911113;
PRIORITY (CC, No, Date): US 612612 901113
DESIGNATED STATES: DE; FR; GB
INTERNATIONAL PATENT CLASS: D02G-003/38; D02G-003/04; A61L-027/00; A61F-002/04; D04C-001/12;

ABSTRACT EP 485986 A1
A synthetic, semiabsorbable composite yarn 10 comprises:
a) a nonabsorbable, elastic core yarn component 12 imparting resiliency to the composite yarn; and
b) at least one absorbable, relatively inelastic sheath yarn component 14 imparting transverse strength to the composite yarn; with said sheath yarn component braided about said core yarn component. (see image in original document)
ABSTRACT WORD COUNT: 60

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	555
SPEC A	(English)	EPABF1	5660
Total word count - document A			6215
Total word count - document B			0
Total word count - documents A + B			6215

4/3,AB/22 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00412218
PHARMACEUTICAL PREPARATION
ARZNEIMITTELZUBEREITUNG
PREPARATION PHARMACEUTIQUE
PATENT ASSIGNEE:
PRISELL, Per, (1245610), Ringvagen 40, 118 67 Stockholm, (SE), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;LU;NL;SE)
NORSTEDT, Gunnar, (1245620), Forfattarvagen 46, 161 42 Bromma, (SE), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
PRISELL, Per, Ringvagen 40, 118 67 Stockholm, (SE)
NORSTEDT, Gunnar, Forfattarvagen 46, 161 42 Bromma, (SE)
LEGAL REPRESENTATIVE:

Bergvall, Stina-Lena et al (22401), Dr. Ludwig Brann Patentbyra AB P.C
Box 17192, 104 62 Stockholm, (SE)
PATENT (CC, No, Kind, Date): EP 444081 A1 910904 (Basic)
EP 444081 B1 990512
WO 9005522 900531
APPLICATION (CC, No, Date): EP 89912690 891117; WO 89SE666 891117
PRIORITY (CC, No, Date): SE 884164 881117
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-009/22; A61K-047/00; A61K-038/00;
A61K-038/27; A61L-027/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9919	270
CLAIMS B	(German)	9919	212
CLAIMS B	(French)	9919	358
SPEC B	(English)	9919	1485
Total word count - document A			0
Total word count - document B			2325
Total word count - documents A + B			2325

4/3,AB/23 (Item 16 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00405241
Fibronectin binding protein as well as its preparation.
Fibronektinbindungsprotein und dessen Herstellung.
Proteine liant la fibronectine et sa preparation.
PATENT ASSIGNEE:
ALFA-LAVAL AGRI INTERNATIONAL AB, (372671), Farm Center P.O. Box 39,
S-147 00 Tumba, (SE), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Hook, Magnus, 121, Stevens Hill Circle, Birmingham, AL 35244, (US)
Jonsson, Klas, Studentvagen 7, S-752 34 Uppsala, (SE)
Lindberg, Kjell Martin, Kornvagen 5, S-752 57 Uppsala, (SE)
Signas, Lars Christer, Hamnesplanaden 2A, S-753 23 Uppsala, (SE)
LEGAL REPRESENTATIVE:
Inger, Lars Ulf Bosson (23194), L + U INGER Patentbyra AB Garvaregatan 12
, S-262 63 Angelholm, (SE)
PATENT (CC, No, Kind, Date): EP 397633 A2 901114 (Basic)
EP 397633 A3 910731
EP 397633 B1 950802
APPLICATION (CC, No, Date): EP 90850166 900504;
PRIORITY (CC, No, Date): SE 891687 890511
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/31; C12P-021/02;

ABSTRACT EP 397633 A2
The present invention relates to a new recombinant hybrid-DNA-molecule comprising a nucleotide sequence from S. aureus coding for a protein, or polypeptide, having fibronectin binding properties.
ABSTRACT WORD COUNT: 30

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	276
CLAIMS B	(English)	EPAB95	70
CLAIMS B	(German)	EPAB95	70
CLAIMS B	(French)	EPAB95	79
SPEC A	(English)	EPABF1	3946
SPEC B	(English)	EPAB95	3931
Total word count - document A			4222
Total word count - document B			4150
Total word count - documents A + B			8372

4/3,AB/24 (Item 17 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00380233
Fibronectin binding protein as well as its preparation.
Fibronektin-bindendes Protein sowie seine Herstellung.
Proteine liant la fibronectine et sa preparation.
PATENT ASSIGNEE:
Normark, Staffan, (1101420), Zackrisvagen 28, S-913 00 Holmsund, (SE), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
Olsen, Arne, (1101430), Sprakgrand 19, S-902 41 Umea, (SE), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Normark, Staffan, Zackrisvagen 28, S-913 00 Holmsund, (SE)
Olsen, Arne, Sprakgrand 19, S-902 41 Umea, (SE)
LEGAL REPRESENTATIVE:
Inger, Lars Ulf Bosson (23194), L + U INGER Patentbyra AB Garvaregatan 12 , S-262 63 Angelholm, (SE)
PATENT (CC, No, Kind, Date): EP 342173 A2 891115 (Basic)
EP 342173 A3 891213
APPLICATION (CC, No, Date): EP 89850142 890502;
PRIORITY (CC, No, Date): SE 881723 880506
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/00; A61K-039/108; A61K-037/00; C07K-003/06;

ABSTRACT EP 342173 A2
The present invention relates to a new fibronectin binding protein from E. coli in the form of a curli pili. a new recombinant hybrid-DNA-molecule comprising a nucleotide sequence from E. coli coding for a protein or polypeptide having fibronectin binding properties.
ABSTRACT WORD COUNT: 45

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	385
SPEC A	(English)	EPABF1	5619
Total word count - document A			6004
Total word count - document B			0
Total word count - documents A + B			6004

4/3,AB/25 (Item 18 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00347393
Novel protein H being capable of binding to IgG, gene coding for said protein H and a process for producing said protein H.
IgG-bindendes Protein H, kodierendes Gen dafur und Verfahren zu seiner Herstellung.
Proteine H, capable de lier IgG, gene codant pour cette proteine, et procede pour sa preparation.
PATENT ASSIGNEE:
SUMITOMO PHARMACEUTICALS COMPANY, LIMITED, (653537), 2-8, Doshomachi 2-chome, Osaka, (JP), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
HighTech Receptor AB, (838040), Skeppsbron 2, S-211 20 Malmo, (SE), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Gomi, Hideyuki, 3-13-30, Hirose Shimamoto-cho, Mishima-gun Osaka-fu, (JP)
Hozumi, Tatsunobu, 3-315, Sonehigashimachi 2-10, Toyonaka-shi Osaka-fu, (JP)
Hattori, Shizuo, 706, Matsukazecho 3-5-3 Suma-ku, Kobe-shi Hyogo-ken, (JP)
Tagawa, Chiaki, 102, Tondacho 3-28-2, Takatsuki-shi Osaka-fu, (JP)
Kishimoto, Fumitaka, 4-8-1, Daiwa Higashi, Kawanishi-shi Osaka-fu, (JP)
Bjorck, Lars, Kornvagen-40, S-240 17 Sodra Sandby, (SE)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100311), Postfach 86 07 67, D-81634 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 371199 A1 900606 (Basic)
EP 371199 B1 941005
APPLICATION (CC, No, Date): EP 89113430 890721;
PRIORITY (CC, No, Date): JP 88295527 881121; JP 8958434 890309
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-013/00; C12N-015/31; G01N-033/566; A61K-037/02;

ABSTRACT EP 371199 A1
A gene coding for Protein H, which is capable of binding specifically to human IgG of all subclasses, was isolated from Streptococcus sp. AP1 and expressed in host cells, E. coli to produce the Protein H
ABSTRACT WORD COUNT: 40

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	772
CLAIMS B	(German)	EPBBF1	690
CLAIMS B	(French)	EPBBF1	873
SPEC B	(English)	EPBBF1	5588
Total word count - document A			0
Total word count - document B			7923
Total word count - documents A + B			7923

4/3,AB/26 (Item 19 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00340177
An adsorber module and adsorber apparatus for whole blood treatment
Adsorbermodul sowie Adsorberapparat zur Behandlung von Vollblut
Module et appareil d'adsorption pour le traitement du sang total
PATENT ASSIGNEE:
ASAHI MEDICAL Co., Ltd., (507231), 1-1 Uchisaiwaicho 1-chome, Chiyoda-Ku
Tokyo, (JP), (Proprietor designated states: all)
INVENTOR:
Kuroda, Toru, 2620 Oaza-Sato, Oita-shi Oita-ken, (JP)
Tohma, Norio, 748 Oaza-Yamauchi Inukai-cho, Ohno-gun Oita-ken, (JP)
LEGAL REPRESENTATIVE:
Strehl Schubel-Hopf & Partner (100941), Maximilianstrasse 54, 80538
Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 341413 A2 891115 (Basic)
EP 341413 A3 900725
EP 341413 B1 931027
EP 341413 B2 000517
APPLICATION (CC, No, Date): EP 89105890 890404;
PRIORITY (CC, No, Date): JP 8881276 880404
DESIGNATED STATES: DE; FR; GB; IT
INTERNATIONAL PATENT CLASS: A61M-001/36; B01D-015/00

ABSTRACT EP 341413 A2
A novel adsorber module for whole blood treatment is disclosed, which comprises a casing provided with a blood introduction means (2) and a blood withdrawal means (3) and a bundle of a plurality of porous hollow fibers (1) disposed in the casing and disposed between and fluid-tightly connected at end portions thereof to the blood introduction means (2) and the blood withdrawal means (3), wherein each porous hollow fiber (1) comprises a membranous porous resin matrix having pores (7) which open at least at the inner wall (5) of the hollow fiber (1) and a plurality of ligands (8) linked to the overall surface, including the walls of open pores (7), of the porous resin matrix. The adsorber module can easily be constructed into an adsorber apparatus which can be practically employed for treatment of whole blood. With this apparatus, whole blood can be effectively, efficiently treated without the danger of blood coagulation and hollow clogging, whereby the malignant components of the whole blood can be effectively removed by adsorption on the ligands (8).
ABSTRACT WORD COUNT: 178

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200020	977
CLAIMS B	(German)	200020	931
CLAIMS B	(French)	200020	1065
SPEC B	(English)	200020	10008
Total word count - document A			0
Total word count - document B			12981
Total word count - documents A + B			12981

4/3,AB/27 (Item 20 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00330086
BIODADHESION DRUG CARRIERS FOR ENDOTHELIAL AND EPITHELIAL UPTAKE AND

LESIONAL LOCALIZATION OF THERAPEUTIC AND DIAGNOSTIC AGENTS
BIOADHASIVER ARZNEITRAGER ZUR ENDOTHELIALEN UND EPITHELIALEN AUFNAHME UND LASIONALEN LOKALISIERUNG THERAPEUTISCHER UND DIAGNOSTISCHER STOFFE
SUPPORT DE MEDICAMENTS A BIO-ADHESION POUR ABSORPTION ENDOTHELIALE ET EPITHELIALE ET LOCALISATION D'AGENTS THERAPEUTIQUES ET DE DIAGNOSTIC

PATENT ASSIGNEE:
Access Pharmaceuticals, Inc., (1415581), 2600 Stemmons Freeway, Suite 210 , Dallas, Texas 75207, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)

INVENTOR:
RANNEY, David F., 3539 Courtdale Drive, Dallas, TX 75234, (US)

LEGAL REPRESENTATIVE:
Dost, Wolfgang, Dr.rer.nat., Dipl.-Chem. et al (3042), Patent- und Rechtsanwalte Bardehle . Pagenberg . Dost . Altenburg . Frohwitter . Geissler & Partner Postfach 86 06 20, D-81633 Munchen, (DE)

PATENT (CC, No, Kind, Date): EP 352295 A1 900131 (Basic)
EP 352295 B1 930616
WO 8807365 881006

APPLICATION (CC, No, Date): EP 88903702 880330; WO 88US1096
PRIORITY (CC, No, Date): US 33432 870401
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-009/16
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB96	1013
CLAIMS B	(German)	EPAB96	997
CLAIMS B	(French)	EPAB96	1278
SPEC B	(English)	EPAB96	13330
Total word count - document A			0
Total word count - document B			16618
Total word count - documents A + B			16618

4/3,AB/28 (Item 21 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00328043
COSMETIC AGENT AND COMPOSITION FOR SKIN TREATMENT.
KOSMETISCHES MITTEL UND ZUSAMMENSETZUNG ZUR BEHANDLUNG DER HAUT.
AGENT COSMETIQUE ET PREPARATION SERVANT AU TRAITEMENT DE L'EPIDERME.

PATENT ASSIGNEE:
KLUDAS, Martin, (1058670), Herthastrasse 22, D-14193 Berlin, (DE), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)

INVENTOR:
KLUDAS, Martin, Herthastrasse 22, D-14193 Berlin, (DE)

LEGAL REPRESENTATIVE:
Patentanwalte Ruff, Beier, Schondorf und Mutschele (100161), Willy-Brandt-Strasse 28, D-70173 Stuttgart, (DE)

PATENT (CC, No, Kind, Date): EP 389470 A1 901003 (Basic)
EP 389470 B1 931118
WO 8905137 890615

APPLICATION (CC, No, Date): EP 88900689 871201; WO 87EP746 871201
PRIORITY (CC, No, Date): EP 88900689 871201; WO 87EP746 871201
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE

INTERNATIONAL PATENT CLASS: A61K-007/48; A61K-007/06;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	411
CLAIMS B	(German)	EPBBF1	354
CLAIMS B	(French)	EPBBF1	530
SPEC B	(English)	EPBBF1	5667
Total word count - document A			0
Total word count - document B			6962
Total word count - documents A + B			6962

4/3,AB/29 (Item 22 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00326995
Protein Arp, with immunoglobulin A binding activity, cloning and expression thereof.
Protein Arp, mit Bindungsaktivitat fur Immunglobulin A sowie dessen Klonierung und Expression.
Proteine Arp ayant une activite liante a l'immunoglobuline A, ainsi que son clonage et son expression.
PATENT ASSIGNEE:
HighTech Receptor AB, (838040), Skeppsbron 2, S-211 20 Malmo, (SE),
(applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Lindahl, Gunnar, Magle lilla kyrkogata 6, S-223 51 Lund, (SE)
Heden, Lars-Olof, Mollevagen 3, S-240 10 Dalby, (SE)
Frithz, Elisabet, Tullgatan 2, S-223 54 Lund, (SE)
LEGAL REPRESENTATIVE:
Fagerlin, Helene et al (22771), H. ALBIHNS PATENTBYRA AB P.O. Box 3137, S-103 62 Stockholm, (SE)
PATENT (CC, No, Kind, Date): EP 367890 A1 900516 (Basic)
APPLICATION (CC, No, Date): EP 88850389 881111;
PRIORITY (CC, No, Date): EP 88850389 881111
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-013/00; C12N-015/31; C12N-015/70; C12N-001/20; C12P-021/02; G01N-033/569; A61K-039/09;

ABSTRACT EP 367890 A1
This invention relates to a new protein called Arp 4 and subfragments thereof with affinity for immunoglobulin A, a process for cloning and expression of the protein, the corresponding vectors and hosts, a process for preparing the organism, a method for preparing the protein, a reagent kit and a pharmaceutical composition comprising the protein or fragments thereof.
ABSTRACT WORD COUNT: 61

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	309
SPEC A	(English)	EPABF1	4602
Total word count - document A			4911

Total word count - document B 0
Total word count - documents A + B 4911

4/3,AB/30 (Item 23 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00277319
An immunoglobulin A receptor protein (Arp), cloning and expression thereof.
Immunoglobulin-A-Rezeptor-Protein (Arp), sowie dessen Klonierung und Expression.
Recepteur d'immunoglobuline A (Arp), ainsi que son clonage et son expression.
PATENT ASSIGNEE:
HighTech Receptor AB, (838040), Skeppsbron 2, S-211 20 Malmo, (SE),
(applicant designated states: AT;BE;CH;DE;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Gunnar, Lindahl, Magle lilla kyrkogata 6, S-223 51 Lund, (SE)
LEGAL REPRESENTATIVE:
Fagerlin, Helene et al (22771), H. ALBIHNS PATENTBYRA AB P.O. Box 3137, S-103 62 Stockholm, (SE)
PATENT (CC, No, Kind, Date): EP 290707 A1 881117 (Basic)
EP 290707 B1 920722
APPLICATION (CC, No, Date): EP 87850160 870513;
PRIORITY (CC, No, Date): EP 87850160 870513
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/31; C07K-015/04; C12N-001/20; C12P-021/00; G01N-033/68; A61K-039/02;

ABSTRACT EP 290707 A1
This invention relates to a new protein called Arp and subfragments thereof with affinity for immunoglobulin A, a process for cloning and expression of the protein, the corresponding vectors and hosts, a process for preparing the organism, a method for preparing the protein, a reagent kit and a pharmaceutical composition comprising the protein or fragments thereof.
ABSTRACT WORD COUNT: 60

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	578
CLAIMS B	(German)	EPBBF1	808
CLAIMS B	(French)	EPBBF1	969
SPEC B	(English)	EPBBF1	4441
Total word count - document A			0
Total word count - document B			6796
Total word count - documents A + B			6796

4/3,AB/31 (Item 24 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00246856
Antigens, antibodies and methods for the identification of metastatic human tumors, and cell lines for producing said antibodies.

Antigene, Antikorper und Verfahren zur Identifizierung humaner metastatischer Tumoren und Zellinien zur Herstellung dieser Antikorper.
Antigenes, anticorps et methodes d'identification de tumeurs humaines metastatiques et lignees de cellules pour la production de ces anticorps.

PATENT ASSIGNEE:
BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM, (266341), Office of General Council, 201 West 7th Street, Austin, Texas 78701, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
Nicolson, Garth L., 2611 Valley Manor Drive, Kingwood, TX 77339, (US)
North, Susan M., 10202 Forum Park Drive, Apt. 100, Houston, TX 77036, (US)
Steck, Peter A., 1800 Holcombe, Apt. 209, Houston, TX 77030, (US)
LEGAL REPRESENTATIVE:
Allard, Susan Joyce et al (27611), BOULT, WADE & TENNANT 27 Furnival Street, London EC4A 1PQ, (GB)

PATENT (CC, No, Kind, Date): EP 240341 A2 871007 (Basic)
EP 240341 A3 890719
EP 240341 B1 940511
APPLICATION (CC, No, Date): EP 87302848 870401;
PRIORITY (CC, No, Date): US 846938 860401
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-015/14; C07K-015/06; C07K-015/00; C12P-021/00; C12N-005/00; C12N-015/00; G01N-033/574; G01N-033/577; C12P-021/00; C12R-001/91

ABSTRACT EP 240341 A2
Disclosed are monoclonal antibodies which react with human tumor cells, particularly metastatic human tumor cells, but not with normal human tissues tested. The monoclonal antibodies are prepared against a 580 kilodalton glycoprotein antigen, designated gp580, which is isolated from either rat or human tumor cells. Methods for isolating the glycoprotein antigen are disclosed as well. Moveover, techniques are disclosed for utilizing these antibodies both in the detection and in the prevention of human tumor lesions.
ABSTRACT WORD COUNT: 79

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	775
CLAIMS B	(German)	EPBBF1	747
CLAIMS B	(French)	EPBBF1	871
SPEC B	(English)	EPBBF1	13679
Total word count - document A			0
Total word count - document B			16072
Total word count - documents A + B			16072

4/3,AB/32 (Item 25 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00218315
Osteogenic use of partially purified bone-inducing factor.
Teilweise gereinigter knocheninduzierender Faktor zur Anwendung in der Orteogenese.

Facteur osteo-inducteur partiellement purifie pour utilisation osteogenique.
PATENT ASSIGNEE:
CELTRIX LABORATORIES, INC., (1342680), 2500 Faber Place, Palo Alto CA 94303, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
Seyedin, Saeid, 9 Sutter Creek Lane, Mountain View California 94303, (US)
Thomas, Thomas, 1560 Adelaide, No. 12, Concord California 94520, (US)
LEGAL REPRESENTATIVE:
Harrison, David Christopher et al (31531), MEWBURN ELLIS & CO 2/3 Cursitor Street, London EC4A 1BQ, (GB)
PATENT (CC, No, Kind, Date): EP 242466 A1 871028 (Basic)
EP 242466 B1 911211
APPLICATION (CC, No, Date): EP 86303011 860422;
PRIORITY (CC, No, Date): EP 86303011 860422
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-003/28; A61K-035/32; A61K-037/02

ABSTRACT EP 242466 A1
A partially purified proteinaceous boneinducing factor of 10,000 to 30,000 daltons is described. It is derived from demineralized bovine bone by extraction with a chaotropic agent, gel filtration, cation exchange chromatography using carboxymethyl cellulose at pH 4.8 and gradient elution with NaCl at 10 mM to about 150 mM.
ABSTRACT WORD COUNT: 53

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	211
CLAIMS B	(German)	EPBBF1	204
CLAIMS B	(French)	EPBBF1	246
SPEC B	(English)	EPBBF1	3607
Total word count - document A			0
Total word count - document B			4268
Total word count - documents A + B			4268

- Author(s)

Set	Items	Description
S6	167	AU=(MICHON, F? OR MICHON F?)
S7	4832	AU=(MOORE, S? OR MOORE S?)
S8	894	AU=(BLAKE, M? OR BLAKE M?)
S9	1009	AU=(LAUDE SHARP M? OR SHARP LAUDE M? OR SHARP LAUDE, M? OR LAUDE SHARP, M? OR SHARP, M? OR SHARP M? OR LAUDE M? OR LAUDE, M?)
S10	9	AU=(LAUDE-SHARP, M? OR LAUDE-SHARP M? OR SHARP-LAUDE, M? OR SHARP-LAUDE M?)
S11	1018	S9 OR S10
S12	1	S6 AND S7 AND S8 AND S11
S13	21	S6 AND (S7 OR S8 OR S11)
S14	5	S7 AND (S8 OR S11)
S15	2	S8 AND S11
S16	8	(S6 OR S7 OR S8 OR S11) AND S2
S17	28	(S12 OR S13 OR S15 OR S16 OR S14) NOT S3
S18	14	RD (unique items)

>>>No matching display code(s) found in file(s): 65, 113

18/3,AB/1 (Item 1 from file: 65)

DIALOG(R)File 65:Inside Conferences

03897685 INSIDE CONFERENCE ITEM ID: CN040959221
Comparison of group B meningococcal conjugate vaccines in adult and infant rhesus monkeys: rPorB versus tetanus toxoid as protein carrier
Fusco, P. C.; Farley, E. K.; Bruge, J.; Danve, B.; Gibelin, N.; *Blake, M. S."**; *Michon, F."**; Schulz, D.
CONFERENCE: International pathogenic Neisseria conference-11th
ABSTRACTS OF THE INTERNATIONAL PATHOGENIC NEISSERIA CONFERENCE , 1998; 11TH P: 150
Paris, EDK, 1998
ISBN: 2842540158
LANGUAGE: English DOCUMENT TYPE: Conference Selected abstracts
CONFERENCE LOCATION: Nice, France 1998; Nov (199811) (199811)

18/3,AB/2 (Item 2 from file: 65)
DIALOG(R)File 65:Inside Conferences

02550486 INSIDE CONFERENCE ITEM ID: CN026596268
Preclinical studies on a recombinant group B meningococcal porin as a carrier for a novel Haemophilus influenzae type b conjugate vaccine
Fusco, P. C.; *Michon, F."**; *Laude-Sharp, M."**; Minetti, C. A. S. A.
CONFERENCE: International Society for Vaccines-Symposium; 1st
VACCINE -GUILDFORD THEN LONDON THEN OXFORD-, 1998; VOL 16; NUMBER 19 P: 1842-1849
Elsevier, 1998
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: Conference Selected papers
CONFERENCE EDITOR(S): Brown, F.; Nara, P. L.
CONFERENCE SPONSOR: International Society for Vaccines
CONFERENCE LOCATION: Leesburg, VA
CONFERENCE DATE: Sep 1997 (199709) (199709)

18/3,AB/3 (Item 3 from file: 65)
DIALOG(R)File 65:Inside Conferences

02126507 INSIDE CONFERENCE ITEM ID: CN022241981
Phagocytic, Serological, and Protective Properties of Streptococcal Group A Carbohydrate Antibodies
Zabriskie, J. B.; Poon-King, T.; *Blake, M. S."**; *Michon, F."**
CONFERENCE: Streptococci and streptococcal diseases: Streptococci and the host -Lancefield international symposium; 13th
ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, 1997; VOL 418 P: 917-920
New York, London, Plenum Press, 1997
ISBN: 0306456036
LANGUAGE: English DOCUMENT TYPE: Conference Selected papers
CONFERENCE EDITOR(S): Horaud, T.
CONFERENCE LOCATION: Paris
CONFERENCE DATE: Sep 1996 (199609) (199609)

18/3,AB/4 (Item 4 from file: 65)
DIALOG(R)File 65:Inside Conferences

02126494 INSIDE CONFERENCE ITEM ID: CN022241859
Combination Conjugate Vaccines against Multiple Serotypes of Group B Streptococci
*Michon, F."**; Fusco, P. C.; D'Ambra, A. J.; *Laude-Sharp, M."**
CONFERENCE: Streptococci and streptococcal diseases: Streptococci and the host -Lancefield international symposium; 13th
ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, 1997; VOL 418 P: 847-850
New York, London, Plenum Press, 1997
ISBN: 0306456036
LANGUAGE: English DOCUMENT TYPE: Conference Selected papers
CONFERENCE EDITOR(S): Horaud, T.
CONFERENCE LOCATION: Paris
CONFERENCE DATE: Sep 1996 (199609) (199609)

18/3,AB/5 (Item 5 from file: 65)
DIALOG(R)File 65:Inside Conferences

01868581 INSIDE CONFERENCE ITEM ID: CN019327048
Candidate *Group"** *a"** *Streptococcal"** *Conjugate"** Vaccine Based on the *Group"** *a"** Polysaccharide
*Michon, F."**; Salvadori, L.; Zabriskie, J.; *Blake, M."**
CONFERENCE: Chemotherapy-International congress; 19th
CANADIAN JOURNAL OF INFECTIOUS DISEASES, 1995; VOL 6; NUMBER SUP/C P: 0664
Pulsus Group, 1995
ISSN: 1180-2332
LANGUAGE: English DOCUMENT TYPE: Conference Abstracts and programme
CONFERENCE LOCATION: Montreal, Canada
CONFERENCE DATE: Jul 1995 (199507) (199507)
NOTE:
Also known as 19ICC. Theme title: 100 years after Pasteur, a new age in chemotherapy

18/3,AB/6 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

14243283 PASCAL No.: 99-0445823
The role of B/T costimulatory signals in the immunopotentiating activity of neisserial porin
MACKINNON F G; YU HO; *BLAKE M S"**; *MICHON F"**; CHANDRAKER A; SAYEGH M H; WETZLER L M
Maxwell Finland Laboratory for Infectious Diseases, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts, United States; North American Vaccine, Inc., Beltsville, Maryland, United States; Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, United States
Journal: The Journal of infectious diseases, 1999, 180 (3) 755-761
Language: English
A T cell-dependent immune response to group C meningococcal capsular polysaccharide (CPS) can be elicited when CPS is conjugated to the class 3 neisserial porin (CPS-porin). Treatment of CPS-porin-immunized mice with B7-2 blocking monoclonal antibody (MAb) caused a dramatic reduction in the

CPS-specific IgG response, treatment with anti-B7-1 MAb had no effect, and concurrent blockade of B7-1 and B7-2 resulted in a synergistic abrogation of the CPS-specific IgG response while the CPS IgM response was unaffected. Anti-CD40L MAb treatment caused a significant reduction of both CPS-specific IgG and IgM levels. In contrast, blockade of CTLA4 interactions resulted in increases in both CPS IgG and IgM responses in CPS-porin-immunized mice. These data support the hypothesis that the ability of neisserial porins to improve the immune response to poorly immunogenic antigens (e.g., polysaccharides) is related to porin-induced increases in B7-2 expression on antigen-presenting cells and enhanced BIT cell interactions.

18/3,AB/7 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

13932619 PASCAL No.: 99-0114868
Multivalent pneumococcal capsular polysaccharide conjugate vaccines employing genetically detoxified pneumolysin as a carrier protein
Vaccines '97/IASIA
*MICHON F"**; FUSCO P C; MINETTI C A S A; *LAUDE-SHARP M"**; UITZ C; HUANG C H; D'AMBRA A J; *MOORE S"**; REMETA D P; HERON I; *BLAKE M S"**
ERSHLER William B, ed
North American Vaccine, Inc., Beltsville, Maryland, United States; Department of Biology and Biocalorimetry Center, The Johns Hopkins University, Baltimore, Maryland, United States
Journal: Vaccine, 1998, 16 (18) 1732-1741
Language: English
A genetically detoxified pneumolysin, pneumolysoid (PLD), was investigated as a carrier protein for pneumococcal capsular polysaccharide (CPS). Such a CPS-PLD conjugate might provide additional protection against pneumococcal infections and resultant tissue damage. A single point mutant of pneumolysin was selected, which lacked measurable haemolytic activity, but exhibited the overall structural and immunological properties of the wild type. PLD conjugates were prepared from CPS serotypes 6B, 14, 19F, and 23F by reductive amination. The structural features of free PLD, as well as the corresponding CPS-PLD, as assessed by circular dichroism spectroscopy, were virtually indistinguishable from the wild type counterpart. Each of the CPS monovalent and tetravalent conjugate formulations were examined for immunogenicity in mice at both 0.5 and 2.0 mu g CPS per dose. Tetanus toxoid (TT) conjugates were similarly created and used for comparison. The resultant conjugate vaccines elicited high levels of CPS-specific IgG that was opsonophagocytic for all serotypes tested. Opsonophagocytic titres, expressed as reciprocal dilutions resulting in 50% killing using HL -60 cells, ranged from 100 to 30000, depending on the serotype and formulation. In general, the lower dose and tetravalent formulations yielded the best responses for all serotypes (i.e., either equivalent or better than the higher dose and monovalent formulations). The PLD conjugates were also generally equivalent to or better in CPS-specific responses than the TT conjugates. In particular, both the PLD conjugate and the tetravalent formulations induced responses for type 23F CPS that were approximately an order of magnitude greater than that of the corresponding TT conjugate and monovalent formulations. In addition, all the PLD conjugates elicited high levels of pneumolysin-specific IgG which were shown to neutralize pneumolysin-induced haemolytic activity in vitro. As a result of these

findings, PLD appears to provide an advantageous alternative to conventional carrier proteins for pneumococcal multivalent CPS conjugate vaccines.

18/3,AB/8 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

12895364 PASCAL No.: 97-0160618
Preclinical evaluation of a novel group B meningococcal conjugate vaccine that elicits bactericidal activity in both mice and nonhuman primates
FUSCO P C; *MICHON F"**; TAI J Y; *BLAKE M S"**
North American Vaccine, Inc., Beltsville, Maryland, United States
Journal: The Journal of infectious diseases, 1997, 175 (2) 364-372
Language: English
Group B meningococcal (GBM) conjugate vaccines were prepared using chemically modified N-propionylated polysialic acid, from Escherichia coli K1 polysaccharide capsule, coupled by reductive amination to tetanus toxoid and purified recombinant GBM porin (rPorB). All conjugates elicited high antibody levels in mice with good booster responses. However, only rPorB conjugates elicited bactericidal activity specific against a broad spectrum of five different GBM serotypes. Bactericial activity was completely inhibited by free N-propionylated polysaccharide. In baboons and rhesus monkeys, rPorB conjugates elicited high antibody titers, with IgG booster responses 9- to 15-fold higher than primary responses. Bactericial activity increased 19- to 39-fold over preimmune values, using rabbit complement; increased bactericial activity was also confirmed with human and monkey complement. IgG cross-reactivity for unmodified N-acetyl polysaccharide was <5% for 79% of mice and <10% for 80% of primates. These studies strongly suggest that the N-propionylated polysialic acid-rPorB conjugate is an excellent vaccine candidate for human use.

18/3,AB/9 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal

12036749 PASCAL No.: 95-0230201
Group A streptococcus-liposome ELISA antibody titers to group A polysaccharide and opsonophagocytic capabilities of the antibodies
SALVADORI L G; *BLAKE M S"**; MCCARTY M; TAI J Y; ZABRISKIE J B
Rockefeller univ., lab. clin. microbiology/immunology, New York NY, USA
Journal: The Journal of infectious diseases, 1995, 171 (3) 593-600
Language: English
Antibodies reactive with *group"** A *streptococci"** (*GAS"**) carbohydrate were studied by ELISA and in an indirect bactericidal assay. The ELISA used *GAS"** carbohydrate covalently *bound"** to phosphatidylethanolamine incorporated into liposomes so that both precipitating and nonprecipitating antibodies were measured. Sera from children from different geographic areas exhibited marked differences in levels of anti-GAS carbohydrate antibody, which increased with age. The antibodies were predominantly of IgG. In bactericidal assays, most of these sera promoted phagocytosis of several type-specific M-positive strains. Opsonization was also related to serum levels of anti-GAS carbohydrate

antibodies. These opsonizing antibodies were depleted from the serum by absorption of the sera on an N-acetyl-D-glucosamine affinity column. Antibody eluted from this column could partially restore opsonization of GAS. Anti-GAS carbohydrate antibodies play a major role in these opsonophagocytosis assays

18/3,AB/10 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal

09018085 PASCAL No.: 90-0186266
Immunogenicity of liposome-*bound"** *hyaluronate"** in mice: at least two different antigenic sites on *hyaluronate"** are identified by mouse monoclonal antibodies
FILLIT H M; *BLAKE M"**; MACDONALD C; MCCARTY M
Rockefeller univ., lab. bacteriology & immunology, New York NY 10029, USA
Journal: Journal of experimental medicine, 1988, 168 (3) 971-982
Language: English

18/3,AB/11 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01066660
PROCEDURES FOR THE EXTRACTION AND ISOLATION OF BACTERIAL CAPSULAR POLYSACCHARIDES FOR USE AS VACCINES OR LINKED TO PROTEINS AS CONJUGATES VACCINES
VERFAHREN ZUR EXTRAKTION UND ISOLIERUNG VON BAKTERIELLEN HULLPOLYSACCHARIDEN ZUR VERWENDUNG ALS VAKZINE ODER, AN PROTEINE GEKOPPELT, ALS KONJUGIERTE VAKZINE
PROCEDURES PERMETTANT D'EXTRAIRE ET D'ISOLER DES POLYSACCHARIDES CAPSULAIRES BACTERIENS DESTINES A ETRE UTILISES SEULS, EN TANT QUE VACCINS OU, LIES A DES PROTEINES, EN TANT QUE VACCINS CONJUGUES
PATENT ASSIGNEE:
NORTH AMERICAN VACCINE, INC., (1439713), 10150 Old Columbia Road, Columbia, MD 21046, (CA), (Applicant designated States: all)
INVENTOR:
*MICHON, Francis"**, 4401 Rosedale Avenue, Bethesda, MD 20814, (US)
*BLAKE, Milan"**, 8521 Beauford Avenue, Fulton, MD 20759, (US
LEGAL REPRESENTATIVE:
von Samson-Himmelstjerna, Friedrich R., Dipl.-Phys. et al (12469), SAMSON & PARTNER Widenmayerstrasse 5, 80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1051506 A1 001115 (Basic)
WO 9932653 990701
APPLICATION (CC, No, Date): EP 98966468 981223; WO 98US27375 981223
PRIORITY (CC, No, Date): US 68608 971223
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12P-019/04; C12P-019/26; C08B-037/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

18/3,AB/12 (Item 2 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

01026643
IMMUNOGENIC CONJUGATES COMPRISING A GROUP B MENINGOCOCCAL PORIN AND AN $i(H. INFLUENZAE) POLYSACCHARIDE
IMMUNOGENE KONJUGATE AUS EINEM GRUPPE B MENINGOKOKKEN-PORIN UND EINEM POLYSACCHARID AUS -I(H. INFLUENZAE)
CONJUGUES IMMUNOGENES RENFERMANT UNE PORINE MENINGOCOCCIQUE DU GROUPE B ET UN POLYSACCHARIDE $i(H. INFLUENZAE)
PATENT ASSIGNEE:
NORTH AMERICAN VACCINE, INC., (1439711), 12103 Indian Creek Court, Beltsville, MD 20705, (US), (Applicant designated States: all)
INVENTOR:
*BLAKE, Milan, S."**, 8521 Beaufort Drive, Fulton, MD 20759, (US)
*MICHON, Francis"**, 4401 Rosedale Avenue, Bethesda East, MD 20814, (US)
FUSCO, Peter, C., 4205 Red Cedar Lane, Burtonsville, MD 20866, (US)
HERON, Iver, , DECEASED, (US
LEGAL REPRESENTATIVE:
Schlich, George William et al (75591), Mathys & Squire European Patent Attorneys, 100 Gray's Inn Road, London WC1X 8AL, (GB)
PATENT (CC, No, Kind, Date): EP 1003549 A1 000531 (Basic)
WO 9903501 990128
APPLICATION (CC, No, Date): EP 98935762 980717; WO 98US14838 980717
PRIORITY (CC, No, Date): US 52952 970717; US 57795 970908
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/102; A61K-039/095; A61K-039/385; A61K-039/116; A01N-043/04; C07K-001/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

18/3,AB/13 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00733926
GROUP A STREPTOCOCCAL POLYSACCHARIDE IMMUNOGENIC COMPOSITIONS AND METHODS
GRUPPE A STREPTOKOKKENPOLYSACCHARIDE IMMUNOGEN-ZUSAMMENSETZUNGEN UND VERFAHREN
COMPOSITIONS DE POLYSACCHARIDES DE STREPTOCOQUES DU GROUPE A AYANT DES PROPRIETES IMMUNOGENES ET PROCEDES ASSOCIES
PATENT ASSIGNEE:
THE ROCKEFELLER UNIVERSITY, (315601), 1230 York Avenue, New York New York 10021-6399, (US), (Proprietor designated states: all)
NORTH AMERICAN VACCINE, INC., (1439713), 10150 Old Columbia Road, Columbia, MD 21046, (CA), (Proprietor designated states: all)
INVENTOR:
*BLAKE, Milan, S."**, 2553 Sylvan Glen Court, Iowa City, IA 52246, (US)
ZABRISKIE, John, B., 1385 York Avenue, New York, NY 10021, (US)
TAI, Joseph, Y., 1370 Cinnamon Drive, Fort Washington, PA 19034, (US)
*MICHON, Francis"**, 9735 Country Meadows Lane, Laurel, MD 20723, (US
LEGAL REPRESENTATIVE:
Vossius, Volker, Dr. (12524), Dr. Volker Vossius, Patentanwaltskanzlei - Rechtsanwaltskanzlei, Holbeinstrasse 5, 81679 Munchen, (DE)

PATENT (CC, No, Kind, Date): EP 754055 A1 970122 (Basic)
EP 754055 B1 000927
WO 9528960 951102
APPLICATION (CC, No, Date): EP 95916479 950420; WO 95US4973 950420
PRIORITY (CC, No, Date): US 231229 940421
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; SI
INTERNATIONAL PATENT CLASS: A61K-039/09; A61K-039/385; A61K-009/127
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200039	1495
CLAIMS B	(German)	200039	1429
CLAIMS B	(French)	200039	1602
SPEC B	(English)	200039	9305
Total word count - document A			0
Total word count - document B			13831
Total word count - documents A + B			13831

18/3,AB/14 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0241947 DBA Accession No.: 1999-12048 PATENT
Extracting capsular polysaccharides from cellular components of Gram-positive and Gram-negative bacteria, useful for production of vaccines against bacterial infection - especially Streptococcus sp.
AUTHOR: *Michon F"**; *Blake M"**
CORPORATE SOURCE: Beltsville, MD, USA.
PATENT ASSIGNEE: North-American-Vaccine 1999
PATENT NUMBER: WO 9932653 PATENT DATE: 19990701 WPI ACCESSION NO.: 1999-418941 (1935)
PRIORITY APPLIC. NO.: US 68608 APPLIC. DATE: 19971223
NATIONAL APPLIC. NO.: WO 98US27375 APPLIC. DATE: 19981223
LANGUAGE: English
ABSTRACT: A method for extracting capsular polysaccharides from cellular components of Gram-negative and Gram-positive bacteria (especially Streptococcus sp.), by reacting the cellular components with a base reagent under basic conditions and separating the capsular polysaccharide from the cellular components, is new. Also claimed is a modified capsular polysaccharide produced by the process involving extracting Gram-negative or Gram-positive bacterial cellular components with a reagent containing a base. The extracted polysaccharides are useful for the production of vaccines containing the polysaccharides alone or conjugated to proteins (e.g. conjugated vaccines) to protect humans or animals against infection, typically by the strain of bacteria from which the capsular polysaccharide was isolated. They are especially used to induce production of antibodies which are cross-reactive with other pathogenic bacteria therefore producing protection against infection by these other bacteria. (52pp)
? log y
27jun02 14:49:10 User219783 Session D1837.2